A YOUNG HUMAN EMBRYO, SHOWING EARLY DIFFERENTIATION OF THE PRIMITIVE STREAK, TOGETHER WITH SOME OBSERVATIONS ON THE EARLY DEVELOPMENT OF THE HUMAN EMBRYO.

by

T. B. JOHNSTON, M.B., Ch.B.

Despite the fact that our knowledge of the normal development of the human embryo in its early stages has increased very substantially in the past twenty years, there are still many points on which further evidence is necessary and which cannot be elucidated until a much larger amount of material is available. The embryo on which this thesis is based is a well-fixed specimen and its detailed description therefore may conceivably contribute a little towards the solution of some of the problems with which the study of Human Embryology is beset.

The embryo represents a slightly later stage of development than the beautifully preserved Strahl-Beneke (1910) specimen, and a slightly earlier stage than the Embryo Hugo (1926), with both of which it will be specifically compared. It corresponds in many ways to Grosser's (1931) Embryo H. Schm.10, but as no detailed description has yet been published of this embryo and only a schematic median section has so far been figured, I can only use it occasionally for purposes of comparison. The subject of this thesis will be referred to as H.R.1, as it was obtained at operation by Mr E. Hesketh Roberts, to whom I am deeply indebted for the specimen and for the following clinical notes on the case.

HISTORY.

The specimen was obtained from the uterus of a woman on whom hysterectomy was performed. She attended the Gynaecological Clinic of St John's Hospital, Lewisham, in February, 1932, complaining of pain in the right iliac and sacral regions. She was found to be suffering from congestive dysmenorrhoea, with mild menorrhagia and marked leucorrhoea, which dated from her last confinement, two years previously, when she had given birth to healthy twins. Prior to that confinement her periods had always been regular every 28 days and had lasted for 5 days, but since then they had increased in duration to 6 or 7 days, although the intermenstrual period remained unaltered. There was no history of previous miscarriages. On examination the uterus was found to be moderately enlarged and the condition was diagnosed as either multiple small fibromyomata or chronic subinvolution, accompanied by an early stage of cystocele. It was decided to perform a subtotal hysterectomy, combined with abdominal cystopexy and she was admitted to Hospital on July 12th, 1932. The first day of the last menstrual period was June 17th. The operation was performed on July 14th. A corpus luteum was found in the right ovary, and, when the uterus was opened after removal, the endometrium was found to be generally and uniformly thickened and congested. It contained a haemorrhagic-looking spot about the size of an ordinary pin's head. The muscular wall of the uterus was slightly thickened. The whole organ was fixed in 5% formalin and subsequently the haemorrhagic spot was removed for

section together with the whole thickness of the underlying uterine wall. A few sections were cut and showed the presence of an early chorionic vesicle. Unfortunately the block was mislaid for some time and it did not come into my possession until November, 1935, when it was no longer possible to obtain any further history or the dates of coitus.

TECHNIQUE.

It proved necessary to re-block the specimen. This was especially unfortunate as the chorionic cavity had already been opened, but the condition of the block left no option. The fresh block was cut into a perfect series of sections at 5μ, and the sections were stained with Mayer's Haemalum and Alcoholic Eosin.

The sections were then drawn at a magnification of 200 and a reconstruction model was made in millimetre board.

The plane of section was somewhat unfortunate. At first I estimated that it made an angle of 10° with the cranio-caudal axis, but I am now of opinion that the angle is not much more than 5° so that the sections are nearly longitudinal (fig. 1.a). In addition, however, the section plane made an angle of approximately 60° with the horizontal plane (fig. 1.b), and this obliquity has increased the difficulties of interpretation, especially at the caudal end of the shield.

THE OVUM IN SITU.

Before the individual features of the embryo are

described, a brief reference may be made to the appearance of a section through the whole ovum in situ. Such a section is shown in fig.2 and the whole depth of the endometrium in fig.3.

The ovum is not deeply implanted but, like the Strahl-Beneke (1910), the Embryo Hugo (Stieve 1926) and many others, projects beyond the surface of the uterine mucosa. The amount of projection measures nearly 2 mm. beyond the level of the surrounding endometrium. An unusually large blood clot covers the central part of the decidua capsularis and obscures the original point of entry. The chorionic cavity is almost triangular in the section, with the slightly blunted apex furthest away from the surface of the mucosa. As usual, the embryo lies in the deepest part of the cavity and its connecting stalk is attached in the apex of the triangle, although this connexion is not shown in the figure.

The implantation is restricted to the stratum compactum, which shows numerous patches of localised oedema. One of the large venous sinuses, described by Bryce (1908), Falkiner (1932), Teacher (1924) and others, is seen cut obliquely deep to the decidua basalis, in the interval between the stratum compactum and the stratum spongiosum. The latter shows the structure characteristic of an early pregnancy. The glands are enormously dilated and full of secretion, and their epithelium shows the familiar "saw-teeth" projections. A few of the glands in the neighbourhood of the ovum contain blood.

A fuller account of the endometrium will be given following the detailed description of the embryo and the discussion of its salient characters.

RECONSTRUCTION MODEL.

As already stated, a reconstruction model of the embryo was made in millimetre board at a magnification of 200. It included the connecting stalk and a portion of the chorion but not the roof of the amnion, which had collapsed on the shield in places.

The most striking feature of the outside of the model is the shape of the embryonic shield. As can be seen in a cast of the right half of the model, which accompanies this thesis, the shield, which is, as usual, more or less oval in outline, is convex dorsally in all diameters. A slight degree of dorsal convexity is not uncommon in the early human embryo, but the degree of curvature is much greater in H.R.1 than it is in the Bi.1 (Florian 1927), the T.F. (Florian 1928), and the Thompson-Brash (1923) Embryos. It is a matter of considerable importance and will receive full consideration at a subsequent stage.

A second, but less important, feature is the presence of a thickened rim of amniotic ectoderm round the cranial and lateral borders of the shield.

The median section of the model shows that the roof of the yolk sac bulges up into the concavity of the ventral surface of the shield (fig.4). At first sight its cavity does not appear to be disproportionately small compared with the size of the embryo. This appearance is misleading and, if the shield

were flat, or approximately flat, the small size of the yolk sac, as witnessed by its measurements (Table on p.66a) would be a very obvious feature.

A wide funnel-shaped diverticulum projects from the caudal surface of the sac and gives off from its summit a relatively long entodermal cord which passes into the connecting stalk (fig.4). This solid cord of cells is the primordium of the allantoic canal.

Hensen's node, which is seen in the median section of the model, lies caudal to the middle of the shield. Its position corresponds fairly closely to the position of the anterior end of the primitive streak in the Strahl-Beneke Embryo, although, prior to the formation of the head- and tail-folds, it is usually situated at or about the middle of the shield. The part of the primitive streak caudal to the node is short and exhibits an early stage of differentiation. It does not extend to the caudal limit of the shield. The head-process is seen extending cranially for a short distance from the deep part of the node.

Cranial to the head-process the roof of the yolk-sac shows a patch of thickened entoderm (fig.4) and evidence will be brought forward to support the view that it represents the primordium of the prochordal plate.

One other feature, visible on the median section of the model, should be mentioned at this stage. The entoderm of the distal end of the allantoic cord comes into continuity with the ectoderm of the amnion immediately caudal to the

shield (fig.4). This represents the cloacal membrane (p. 41).

The connecting stalk passes from the caudal end of the embryo to the chorion. On its right side, close to its embryonic attachment, it is marked by a deep groove, which is continuous at its right extremity with a tear into the amnion - not shown in the model. This groove, owing to the nature of its walls, was regarded at first as a natural feature, but further consideration led to the conclusion that it was an accidental tear. This discovery served to remove two difficulties which have not yet been mentioned. (1) The attachment of the allantoic cord to the yolk-sac lies considerably to the left of the median plane, as will be shown in the description of the individual sections, and the cord itself shewed an angled bend. (2) The yolk-sac is not symmetrically disposed with reference to the median plane, but projects more to the left than to the right side.

The identification of the groove as an accidental tear made it clear that the embryonic end of the connecting stalk had become slightly kinked on the rest of the stalk and had swung the more ventral part of the yolk-sac over to the left.

MEASUREMENTS.

The following measurements of the embryo are also included in the Table on p.66a, where they are shown in comparison with the corresponding measurements of a number of embryos in related developmental stages. They are included

here for convenience of reference. The measurements of the shield were made over the curvatures.

Chorionic cavity	1.95 mm X 1.36 mm X 1.86 mm+ (Owing to the fact that an unknown number of sections of the chorion had been made before the specimen came into my hands, the last diameter of the cavity is uncertain).
Embryonic shield (excluding the cloacal membrane)	L = .55 mm W = .43 mm
Primitive streak (including Hensen's node)	.115 mm
Hensen's node	L = .06 mm W = .03 mm Depth = .05 mm
Head process	L = .04 mm
Prochordal plate	L = .075 mm
Cloacal membrane	L = .1 mm
Yolk-sac cavity	.35 mm X .23 mm X .3 mm
Villi	.2 mm (on decidua capsularis) .6 mm (on decidua basalis).

Owing to the partial collapse of the roof of the amnion on to the shield and to the curvature of the shield, the measurements of the amniotic cavity are valueless for purposes of comparison and are not included.

BRIEF DESCRIPTION OF THE INDIVIDUAL SECTIONS.

The sections pass through the embryo from its left to its right side. Owing to the obliquity of the section plane (p. 3.), the sections pass at first through the left and ventral walls of the yolk-sac, and it is not until the twenty-first section is reached that the embryonic shield appears.

Owing to the angulation with the median plane (fig.1) the sections cut the median plane of the shield at its caudal end first. The individual slides are numbered serially and twelve sections are mounted on each.

The first section through the primary mesoderm on the left wall of the yolk sac appears in 16.4, but it is not until 16.10 that the cavity of the sac is opened into freely. The left edge of the amnion appears in 17.12, and the edge of the embryonic shield in 18.1. Sections 16.4 - 17.12 are not figured.

18.1 (fig.5). The left edge of the embryonic shield and the left margin of the amnion are seen but the amniotic cavity is not yet opened. It lies in the figure to the left of the yolk-sac, which shows a short, wide diverticulum from the ventral end of its caudal wall (upper end in the photograph). Blood-islands are present on the ventral and cranial walls of the sac. The entodermal cells show a variety of forms.

18.3 (fig.6). The amniotic cavity is apparent and the caudal diverticulum of the yolk-sac has increased in length. A few strands of intraembryonic mesoderm are apparent. In view of the condition found in later sections it should be noted that the primary mesoderm on the cranial end (lower end in the photograph) of the amnion passes straight on to the surface of the yolk-sac.

18.4 (fig.7). The shield has elongated, especially at its caudal end. The caudal diverticulum of the yolk-sac is a little longer and a little narrower.

18.5 (fig.8). Both changes noted in the preceding section are progressing. In addition the intraembryonic mesoderm forms an almost continuous layer over the caudal half or more of the embryonic area, and at its caudal limit its cells are continuous with those of the primary mesoderm. The cells lining the yolk-sac are of at least three different types: (a) On the ventral wall they are cubical or low columnar. (b) On the cranial wall they form a syncytial ribbon. (c) In the roof they are elongated and flattened.

18.6 (fig.9). The caudal diverticulum of the yolk-sac is longer and narrower and shows a distinct bend, concave dorsally. The cells at its apex and on its ventral wall are large and cuboidal, while those on its dorsal wall are more elongated and flattened. Dorsal to the diverticulum the entoderm on the caudal wall of the yolk-sac shows an area of apparent thickening. This appearance is repeated in the ensuing four or five sections, and is regarded as being due to a wrinkling of the wall of the yolk-sac associated with the kinking due to the tear in the connecting stalk. A similar explanation is offered for the additional cells which lie between the primary mesoderm and the caudal wall of the yolk-sac. The intra-embryonic mesoderm covers nearly the whole of the embryonic area, and consists of elongated cells with branching and anastomosing processes.

18.8 (fig.10). All the features noted in 18.6 are present and the indications of wrinkling in the caudal wall of the yolk-sac are more marked. The intra-embryonic mesoderm

establishes continuity with the primary mesoderm at the cranial end of the shield. In this situation the exocoelom threatens to encroach on the embryonic area, and the encroachment becomes real in the succeeding sections.

18.9 (fig.11). At its caudal end the shield ectoderm and the amnion are cut obliquely, foreshadowing a further extension of the shield in a caudal direction. The part of the caudal diverticulum of the yolk-sac which lies distal to the bend already noted has become much narrower. At the cranial end of the shield the exocoelom encroaches into the embryonic area.

18.10 (fig.12). The shield has extended further in a caudal direction, and is cut obliquely at its caudal end; in this situation the shield ectoderm appears to be contributing to the formation of the intra-embryonic mesoderm. The narrow recess at the distal end of the caudal diverticulum of the yolk-sac has just lost its connexion with the interior of the sac. In the cranial part of the sac a group of entodermal cells is apparently lying free; they are part of a large wrinkle in the cranial wall of the sac which can be identified in the succeeding six sections.

18.11 (fig.13). A further extension of the shield in the caudal direction is apparent. A large patch of cells, clearly ectodermal in origin, lies ventral and caudal to the caudal end of the shield. In part this patch represents an oblique shaving through the shield ectoderm, but in part it appears to be forming intra-embryonic mesoderm. The recess of

the caudal diverticulum of the yolk-sac has disappeared; its apex has given rise to a solid cord of entodermal cells which is cut transversely as it lies in the left part of the attachment of the connecting stalk to the embryo. Well-marked wrinkles are present in the cranial and caudal walls of the yolk-sac. The encroachment of the exocoelom on the embryonic area is quite definite.

18.12 (fig.14). Further extension of the shield in a caudal direction is indicated by the oblique shaving through the left wall of the amnion at the caudal end. The solid entodermal cord, which is regarded as the allantoic representative is seen cut transversely, as in the preceding section. Above it in the figure a few cells are visible; they are part of the connecting stalk and the interval between them and the part which contains the allantoic cord is due to the bend associated with the tear in the connecting stalk.

19.1 (fig.15). Owing to an inequality of the floating out of the sections the curvature of the shield is less pronounced on slide 18 than it is on slide 19 and the succeeding slides. The shield continues to extend in a caudal direction and the edge of the shield and the left wall of the amnion are again cut very obliquely at the caudal end of the embryo. In this situation two groups of cells are seen growing out from the deep surface of the ectoderm and occupying the gap between it and the roof of the yolk-sac. Their significance is uncertain. The condition of the connecting stalk is unchanged. It still consists of two portions, one of which

(the lower in the figure) contains the allantoic cord. At the cranial end of the embryonic area the encroachment of the exocoelom is deep and > - shaped.

19.2 (fig.16). No important changes are present in this section. A small, shallow depression on the dorsal surface of the shield, which is present also in the succeeding section and then disappears, has no ascertainable significance. Two mesodermal cells are present in the > - shaped encroachment of the exocoelom. In this situation the condition is not easy to interpret until section 19.6 is reached.

19.3 (fig.17). The amniotic cavity has extended further in a caudal direction and the caudal extension of the shield has almost reached its maximum. A beautiful mitotic figure is seen in the superficial part of the shield near its caudal end. The two parts of the connecting stalk have now come together, so that the section passes through the floor of the bend on the left surface of the stalk. In this section the roof of the amniotic cavity in its middle third shows an appearance almost identical with the appearance of the ventral part of the cranial wall of the yolk-sac in this and other sections. It is impossible to satisfy oneself that it really consists of two layers of cells for the two appear to be fused together to form a syncytial ribbon. Reference will be made to this appearance at a later stage. At the cranial end of the shield the intra-embryonic mesoderm shows traces of cavity formation and it is impossible to be certain whether or not the spaces communicate with the exocoelom.

19.4 (fig.18). Near its caudal limit the ventral surface of the shield ectoderm loses its sharp contour, which is so striking in its cranial two-thirds, and a small mass of cells is growing out from its deep surface in a caudal direction. The sections are now rapidly approaching the median plane and these cells are regarded as derivatives of the end-node of the primitive streak. Attention should be drawn to the irregularly $<$-shaped gap which separates the connecting stalk from the primary mesoderm on the dorsal surface of the caudal diverticulum of the yolk-sac. A few detached cells occupy the gap, which represents the deepest part of the furrow described on the right side of the connecting stalk in the reconstruction model. The gap is more obvious in the later sections and has already been interpreted as an accidental artefact. At the cranial end of the shield the intra-embryonic mesoderm contains further and more obvious signs of cavity formation. A large blood island is present on the ventral wall of the yolk-sac.

19.5 (fig.19). The shield has now reached its full extent at its caudal end, and it is to be noted that in that situation the shield ectoderm consists of only a single layer of cuboidal cells. The end node of the primitive streak is seen .08 mm. from the caudal end of the shield. Its constituent ectoderm is thicker than the ectoderm of the rest of the shield and its ventral border is irregular, showing no trace of a basement membrane. There is no break in the continuity of the underlying entoderm. From the caudal end of

the node cells are growing caudally into the connecting stalk, the tear in which is now more obvious. The allantoic cord is now cut obliquely as it bends towards the section plane. At the cranial end of the shield the intra-embryonic mesoderm shows extensive cavity formation and its continuity with the primary mesoderm is again obvious. The exocoelom no longer encroaches on the embryonic area A small vascular space, best seen in 19.6, is present in the blood island on the ventral wall of the yolk-sac.

19.6 (fig.20). At its caudal end the shield is now reduced to a single layer of flattened cells, over an area .05 mm. long. The end node of the primitive streak and the cells which it contributes to the connecting stalk are clearly seen. The allantoic cord is now cut in its long axis, or nearly so. As before, its outline is sharp except at its ventral end where there is an appearance which suggests active growth towards the ectoderm in the angle between the amnion and the extreme caudal limit of the shield. This is the first indication of the cloacal membrane. At the cranial end a large cavity is now apparent in the intra-embryonic mesoderm. Cranially its walls meet and become continuous with the primary mesenchyme. This cavity is regarded as a precocious coelomic formation. Caudal to it a small patch of thickened entoderm is adherent to the basement membrane of the shield ectoderm.

19.6 (fig.21). The precocious coelomic cavity and the adjoining parts of the embryo are shown at a magnification of 950. It is significant that whereas traces of cytodesmata are visible connecting the one wall to the shield ectoderm and

the other to the roof of the yolk-sac, there is no evidence of any such connexions across the cavity itself. With the exception of one rounded cell all the cells in the walls of the cavity are elongated and typical mesoblasts.

19.7 (fig.22). The flattened cells at the caudal end of the shield are shrunken and in the underlying mesoderm a small gap indicates a continuation of the tear which in the ensuing sections breaks through into the amniotic cavity. The allantoic cord is again cut in its long axis in the connecting stalk. Its apex and caudal (right-hand) border are sharply delimited from the overlying primary mesenchyme, but its cranial (left-hand) border, especially in its ventral (lower) part is very indefinite and in this region the entodermal cells are in continuity with the cells which are interposed between them and the amniotic cavity and which are regarded as a thickening of the amniotic ectoderm. This ecto-entodermal continuity is identified as the cloacal membrane. In the dorsal and cranial (upper and left-hand) part of the connecting stalk a rounded mass of cells, suggestive of a large blood-island, also represents part of the ectodermal constituent of the cloacal membrane, as will be apparent in the succeeding two sections. Cells derived from the end node of the primitive streak are still apparent and, slightly nearer to the cranial

end, a large mass of clumsy looking cells is growing headwards from the primitive streak. This mass, which is .03 mm long, seems to be devoid of entoderm on its ventral surface. It is equally conspicuous in the next section, scarcely recognisable in the next but one, and thereafter disappears. Cranial to this outgrowth the shield is slightly thickened and its ventral surface is irregular and woolly. This represents the first shaving through the left border of Hensen's node. At the cranial end of the shield the precocious coelomic cavity is again conspicuous and caudal to it the entoderm of the yolk-sac is adherent to the basement membrane of the shield ectoderm, although no thickening is apparent. The presence of a desquamated entodermal cell should be noted lying free in the yolk-sac below the middle of the shield.

19.7 (fig.23). The outgrowth from the primitive streak and the adjoining shaving through the left border of Hensen's node are shown X 950. The outgrowth is obviously directly continuous with the ectoderm of the streak.

19.8 (fig.24). The tear at the caudal end has now passed through the shield into the amniotic cavity. The

allantoic cord is not so easy to recognise. Its caudal border (right border in the figure) is still sharp except at its middle, but its ventral border becomes directly continuous with the adjoining cells, which are ectodermal in origin, derived from the adjoining part of the amnion. This is undoubtedly the cloacal membrane. The rounded mass of cells observed in the dorsal and cranial part of the connecting stalk in the preceding section is continuous ventrally, in this and in the next section, with the ventral part (lower part in the figure) of the cloacal membrane. At its narrow, caudal end the appearances suggest continuity with the apical part of the allantoic cord, and this appearance is confirmed in the next section. In this section, therefore, the connecting stalk, with the exception of its covering layer of primary mesenchyme, consists almost entirely of the cloacal membrane. The end node of the primitive streak is no longer visible, but the outgrowth from the streak in a headward direction is again apparent. At its cranial end this outgrowth reaches the caudal surface of Hensen's node, which now involves the whole thickness of the embryonic area. The sharp ventral contour of the shield ectoderm stops very abruptly at the cranial limit of the node. The characteristic structure of the node is seen better in sections 19.10 and 19.11. The condition of the roof of the yolk-sac immediately cranial to the node is difficult to interpret. It is formed by a number of low columnar cells which

appear to be continuous caudally with the deep part of the node. Attention should be drawn to a large round entodermal cell, with a deeply pycnotic nucleus, which is lying free in the yolk-sac in this situation, and to the fact that more cranially the entoderm seems to stop abruptly at a cell which shows a good mitotic figure. The low columnar cells are regarded as forming the left edge of the primordium of the head process. Between them and the ectoderm a group of five mesodermal cells is interposed. These cells really lie to the left of the head process but appear to lie dorsal to it owing to the obliquity of the section plane. At the cranial end of the shield the coelomic cavity, though present, is in two parts and is not so convincing as it was in the two preceding sections. Caudal to it the entoderm is still adherent to the shield ectoderm, although there is no localised thickening.

19.9 (fig.25). In the connecting stalk the entoderm of the allantoic cord is now cut in two places. The larger, proximal portion forms a > -shaped, darkly stained strip, with the concavity facing the amnion. The concavity of the > is occupied by the ectodermal thickening of the amnion. The distal part of the cord, also darkly stained, is directly continuous cranially with the large group of round cells noted in the previous section. The outgrowth from the primitive streak immediately caudal to Hensen's node is still present but it is much smaller. The node itself is larger as the sections at this level are close to the median plane. The roof of the yolk-sac cranial to the node is formed by a number of low

columnar cells, which are not so obviously in continuity with the node owing to the presence of a shrinkage interval. Their nuclei are large and darkly stained, resembling in every way the nuclei in the node. They are separated from the shield ectoderm by a group of three slightly elongated mesoderm cells which also appear to be derived from the node. At the cranial end the precocious coelomic cavity is again present and well formed. Caudal to it the entoderm is again adherent to the shield ectoderm. In this situation it is slightly thickened and consists of a number of large, vesiculous cells with round nuclei.

19.10 (fig.26). The remains of the cloacal membrane are still seen occupying most of the connecting stalk, but in its caudal part there is a greatly increased number of mesenchymal cells. Hensen's node is cut approximately in its median plane. It involves the whole thickness of the embryonic area and no entodermal cells are present on its ventral surface. The pallor of the node is very striking. This is due in part to the fact that its nuclei tend to be grouped into oblique, overlapping rows*, leaving wide areas of non-nucleated cytoplasm, and in part to the fact that the cytoplasm stains rather faintly and contains shrinkage spaces. From the cranial surface of the deep part of the node the primordium of the head process extends cranially. It now consists of five narrow, columnar cells which form the roof of the yolk-sac and extend almost to the basement

*A similar arrangement of the nuclei in the ferret embryo can be seen in some of the figures recently published by Hamilton (1937).

membrane of the shield ectoderm. A shrinkage gap separates the most cranial of these cells from two smaller cells, obviously of the same character, although they are not typically columnar in shape. The nuclei of all these cells of the head process stain darkly, showing a prominent nucleolus, and are identical in appearance with the nuclei in the deep part of the node. From the caudal surface of the node typical mesodermal cells grow caudally between the ectoderm and the entoderm. A single, desquamated entodermal cell is present in the cavity of the yolk-sac ventral to the node. At the cranial end of the embryo the precocious coelomic cavity is here reduced to a slit with slightly thickened walls. Caudal to it the entoderm shows a large thickened patch of vesiculous cells and is again adherent to the shield ectoderm. This is regarded as the primordium of the prochordal plate and will be referred to under that name.

19.11 (fig.27). The last traces of the cloacal membrane are visible in the connecting stalk. Hensen's node and the head process are readily recognisable. From the caudal surface of the node mesenchymal cells are extending caudally between the ectoderm and the entoderm. Two desquamated entodermal cells lie free in the yolk-sac (below the caudal part of the node in the figure). At the cranial end of the embryo the coelomic cavity is obscured, but caudal to it the prochordal plate is a conspicuous feature.

19.11 (fig.28). Hensen's node is shown X 950. The wide areas of non-nucleated cytoplasm and the crowding together of the nuclei are well shown. The node contains a mitotic

figure near its centre. The head process consists of five columnar cells and a mitotic figure is present on its ventral surface at its nodal end. Cranial to these columnar cells there are three smaller cells, whose nuclei show the same staining affinities as the nuclei of the node; they probably represent the headward end of the process.

19.12 (fig.29). Caudally the tear in the shield has led to the sagging away of the connecting stalk. The cloacal membrane has disappeared, and a mass of mesodermal cells occupies the site of its more ventral portion. Hensen's node, which is divided near its right border, is very conspicuous. A shrinkage gap occurs at the cranial end of the head process. The structure of the node and head process are shown X 950 in figure 30. At the cranial end of the embryo the intra-embryonic mesoderm is in process of cavity formation, and the ventral cells show the "syncytial ribbon" appearance already noted in the roof of the amnion and the cranial wall of the yolk-sac. The prochordal plate stands out prominently; its detailed structure is shown X 950 in figure 31.

19.12 (fig.30). The nuclei in Hensen's node are arranged in two oblique, overlapping rows, directed cranially and ventrally. They are not remarkable for their size. The head process consists of three or four columnar cells which occupy nearly the whole space between the shield ectoderm and the roof of the yolk-sac. There is obvious tissue continuity between the caudal end of the process and Hensen's node.

19.12 (fig.31). The prochordal plate consists of about ten large, vesiculous, entodermal cells. Their nuclei do not stain darkly and appear oval in shape in this section. The plate is adherent to the basement membrane of the shield ectoderm over a considerable area.

20.1 (fig.32). The mass of mesodermal cells seen in the connecting stalk in the preceding section is again prominent. Only the dorsal part of Hensen's node is cut, as the section passes close to its right border. Cranial to it the interval between the ectoderm and the yolk-sac is occupied for .03 mm by cells which may be regarded as forming the right edge of the head process. At the cranial end of the embryo the intra-embryonic mesoderm contains a very distinct cavity, which is less extensive in the cranio-caudal axis than it is in some of the preceding sections. Its walls are beautifully fixed and show the "syncytial ribbon" appearance. Caudal to it the prochordal plate is a conspicuous feature.

20.1 (fig.33). The prochordal plate is only adherent to the shield ectoderm at one point. It is of approximately the same thickness as the shield and comprises fourteen or fifteen large vesiculous cells with spherical or oval nuclei; which display a prominent nucleolus and a fine chromatin network. A fine coagulum extends into the yolk-sac from the ventral surface of the plate.

20.2 (fig.34). Unfortunately in this section the connecting stalk has floated away from the embryo and has become so wrinkled that its structure cannot be examined. The last

trace of Hensen's node is seen as a pallid area in the most dorsal part of the shield. Cranial to it mesenchymal cells fill up nearly the whole interval between the shield ectoderm and the yolk-sac, the roof of which is again entodermal. Clearly these cells lie on the right side of the head process and may belong to, or may be derivatives of it. At the cranial end of the embryo the precocious coelomic formation appears for the last time. The prochordal plate is no longer adherent to the ectoderm. In this and in the preceding section (fig.33) there is an extensive wrinkling of the wall of the yolk-sac where the roof becomes continuous with the cranial wall.

20.3 (fig.35). The sections have now reached the right margin of the caudal end of the shield. The angled recess at the dorsi-caudal end of the amniotic cavity is being partially filled up from its right side, as the section is shaving obliquely through the amniotic covering of the connecting stalk. The recess disappears in the ensuing sections. The prochordal plate is easily identified, but some mesoderm cells now intervene between it and the ectoderm. Elsewhere a false appearance of entodermal thickening is presented in the roof of the yolk-sac. This is due to the fact that the sections are now rapidly approaching the right wall of the sac, which is cut obliquely in several places. The wrinkling of the cranial wall at its junction with the roof gives rise to a very exuberant infolding in this section. The succeeding sections pass through the embryo with increasing degrees of obliquity and are entirely to the right of the median plane. As the median plane struc-

tures of the shield are no longer divided, only selected sections from the rest of the series will be figured.

20.8 (fig.36). This section shows a substantial shaving through the right wall of the yolk-sac, which appears as an island of solid entoderm within the concavity of the shield. The connecting stalk, now approaching the chorion, is looser in texture and shows the presence of a number of vascular spaces.

20.10 (fig.37). This section, after dividing the shield, passes through the interval between its right sloping surface and the right wall of the yolk-sac. The interior of the concavity of the shield is occupied by the branching, interconnected cells of the intra-embryonic mesoderm, and the general continuity of the open meshwork of the mesoderm is well demonstrated. In many places the shield ectoderm appears to be giving origin to mesoderm cells, but, owing to the obliquity of the section too much stress must not be laid upon this appearance. A well-formed vascular space, lined by flattened elongated cells, is seen in the connecting stalk (upper and left part in the figure). Other, less convincing, spaces are also present.

From this point onwards, owing to the curvature of the shield and the obliquity of the section plane, the sections through the shield ectoderm become more and more nearly tangential.

21.4 (fig.38). This section cuts through the right surface of the shield tangentially so that it appears as a solid

mass of ectoderm. The connecting stalk is very loose in texture and has almost reached the chorion.

21.10 (fig.39). This section shaves through the right surface of the upturned rim of the amnion to the right of the right border of the shield. The connecting stalk is now in continuity with the primary mesenchyme of the chorion. Both the stalk and the cavity of the amnion can be recognised in the succeeding sections.

Now that the reconstruction model and all the important individual sections have been described, it is possible to discuss the salient features of the embryo and the problems arising from them.

THE EMBRYONIC SHIELD.

In most well preserved human embryos at or near the stage of development exhibited by H.R.1. the shield is flat or very gently convex dorsally, and one is tempted to suggest that the curvature of H.R.1. is the result of slight compression during fixation. Such an explanation, however, is insufficient to account for the condition in its entirety. In the first place the shield is convex in both its longitudinal and its transverse diameters and no degree of compression could bring about this double curvature without causing excessive tearing or wrinkling of the surface of the shield. Apart from the small tear at the caudal end, which is quite incapable of accounting for the condition, the shield is intact and shows no sign of wrinkling. In the second place the yolk-sac shows all the appearances that might be expected if the curvature were the result of a growth

process. Its dome-shaped roof is everywhere adapted to the curve of the shield and shows no sign of wrinkling or tearing.

On these two grounds I believe that the curvature of the shield is the result of abnormal growth, though it is probable that it has been exaggerated to some extent during the process of fixation. Attention has already been drawn to the fact that the embryo was situated in the deepest part of the chorionic cavity, which in this case is the narrowest part of the space. It is not unlikely that the confinement of the embryo in this restricted space may have helped to account for its abnormal shape.

One would not, however, be justified on this account in discounting entirely the importance of the evidence which this embryo offers with regard to other developmental problems, for abnormalities of shape are by no means uncommon. The shield of the Strahl-Beneke embryo is concave dorsally (fig.40), while in the Bi.1, the T.F. and the Hensen (1932) it is convex like the shield of H.R.1., but nevertheless, all these embryos have provided important contributions to our knowledge of the normal development of the human embryo in its early stages.

The shield ectoderm consists of high columnar cells, arranged usually in three, though occasionally in four and sometimes in two, overlapping rows. The cells, for the most part, are set at right angles to the free surface, but in many places their long axes are oblique (fig.31), a fact which may be regarded as confirming the view that the shield curvature is the result of growth processes. At its caudal end the shield ectoderm is abruptly reduced to a single layer of rather

flattened cells over a length of .06 mm. This reduction in thickness is present in both the Strahl-Beneke and the Hugo embryos, and in both it extends as far caudally as the cloacal membrane. Further reference will be made to this feature when the primitive streak is discussed.

The cytoplasm of the cells of the ectoderm stains darkly and the nuclei, which are elongated or oval for the most part, show a rich chromatin network and a prominent nucleolus. In the surface layer numerous cells occur with enlarged, almost spherical nuclei, the cytoplasm of which is less darkly stained. These may possibly be cells which are about to undergo mitosis. In most of the sections mitotic figures are present, the cells concerned being, with few exceptions, situated in the most superficial layer. Only one was found in the caudal part of the shield but three were observed in the depths of Hensen's node. This distribution of mitotic figures agrees well with the condition found in both the Hugo and the Strahl-Beneke embryos, and may be regarded as indicative of rapid increase of size of the pre-nodal part of the shield. It is also clear that enlargement of the shield at this stage is brought about by the division of the cells of the superficial layer.

Intracellular darkly staining droplets are a very striking feature in most of the sections (fig.28). They vary considerably in size and are found at all depths from the surface, being most numerous in the cranial two-thirds of the shield and in the region of Hensen's node. In places the

droplets run together, forming crescentic figures, and they are usually surrounded by a small area of lightly stained cytoplasm. Droplets, identical in appearance, are found within the cavity of the amnion (figs. 19 and 27) and their presence there in considerable quantity suggests that they may be of the nature of an excretion. They have been observed by Florian in the Embryo Fetzer (1929).

No signs of degenerative changes were seen in the superficial cells of the shield. Von Möllendorff (1921) described such changes in the Embryo O.P. and regarded them as normal. Stieve (1926) opposed his interpretation, and the evidence available from H.R.1. strongly supports his view.

Except in the regions of Hensen's node and the primitive streak, the deep surface of the shield ectoderm is sharply demarcated, and the appearance is strongly suggestive of the presence of a basement membrane. Graf Spee (1926) was the first to describe the existence of such a membrane, and it has been identified more recently by von Möllendorff (1921), Rossenbeck (1923), Ramsey (1937), and others, so that it may be regarded as a normal structure. In H.R.1 the shield shows the presence of many, fine, obliquely vertical slits which are the result of shrinkage during fixation. These slits are visible in many of the figures and it is to be noted that, although in some places they reach the basement membrane, they do not break through it. In von Möllendorff's Embryo O.P. the basement membrane was partially detached, a fact which Stieve (1926) regards as indicative of poor fixation. In no situation is

the basement membrane detached in H.R.1.

At the cranial border of the shield and along each lateral border the transition from the shield ectoderm to the typical, flattened epithelium of the amnion is gradual. As a result the shield appears to have a turned-up rim everywhere except at its caudal end. This rim is regarded as part of the amnion and has been excluded in estimating the measurements of the shield. It bears no relation to the entoderm of the yolk-sac and the primary mesoderm passes continuously from its outer surface on to the cranial and lateral walls of the sac. A similar rim is present along the lateral margins of the Fetzer Embryo (Florian, 1936), and in the Strahl-Beneke (fig.40). The transition from shield to amnion at the cranial end is so gradual that it is difficult to determine the precise cranial limit of the embryonic area.

Streeter (1936) has recently put forward the view that the first and most fundamental differentiation in the morula mass separates the cells which take part in the formation of the embryo itself from those which form only extra-embryonic structures. Amongst the latter he includes the cells of the amnion and as evidence in favour of this view he cites the abrupt character of the transition from the shield ectoderm to the ectoderm of the amnion. This view will be considered later in connexion with the yolk-sac, but from the embryos cited it is clear that the transition from shield ectoderm to amniotic ectoderm may be either gradual or abrupt, and that its character cannot be adduced as evidence in support of Streeter's view.

THE PRIMITIVE STREAK.

The primitive streak, including Hensen's node, has been identified in sections 19.4 - 20.2. It measures .115 mm in length and its caudal end falls short of the caudal end of the shield by .09 mm.

The cranial half, or rather more, of the streak can readily be distinguished from its caudal half. It stands out as a relatively pale area in the darkly stained shield (fig.26) and shows features which indicate that it may justly be regarded as an early stage of Hensen's node. At its cranial surface the sharp contour of the deep surface of the shield ectoderm ceases abruptly, and there is tissue continuity through the whole thickness of the embryonic area, the entoderm being absent from its ventral surface. The structure of the node has already been described and reasons have been given for its characteristic pallor, (p.19). In older embryos, such as the Manchester embryo (Hill and Florian, 1935), the contrast between the pallor of the node and the dark staining of the adjoining primitive streak is sometimes very striking. No such contrast, however, is present in the figures of the Embryo Hugo or Strahl-Beneke, and a very similar pallid area in the Fetzer is regarded by Florian as the primitive streak itself prior to node formation. No surface elevation marks the position of the node, but, although Stieve lays stress on its presence as a means of identification, it is clear from Embryo Bi.24 that a typical node may be present with little or no surface elevation. In older embryos, the surface elevation is more constant. In

identifying the pallid area in H.R.1 as Hensen's node, I have been more influenced by the fact that it is giving rise to the primordium of the head process.

The primitive streak proper is very short, measuring only .055 mm long. It is in an early stage of differentiation and does not yet extend to the cloacal membrane, being separated from it by a zone of undifferentiated ectoderm, .09 mm long. The constituent cells of the streak are wider than those of the rest of the shield ectoderm and have large oval nuclei. They are packed closely together and few shrinkage slits, such as have been described on page 28, can be seen. The cytoplasm of the cells stains darkly and no difficulty is experienced in determining where the streak ends and Hensen's node begins. At its caudal end the deep surface of the streak gives origin to a group of cells (fig.20) which stream into the connecting stalk. These cells are, I believe, identical with those described by Stieve as forming the "sichel-knoten" in the Embryo Hugo and by Florian as the "end node" in the Strahl-Beneke. They must be regarded as characteristic of the early stages of the primitive streak, but no light has yet been thrown on their significance.

The small mass of large ectodermal cells which springs from the cranial end of the streak proper (fig.23) is difficult to interpret, for the cells do not appear to be mesodermal, as they retain their ectodermal characters unchanged. The only approximately parallel appearance which I have been able to find in the literature is in the Meyer (1924) Embryo,

where it was identified - wrongly according to Florian (1929) - as the head process. If the two structures are actually identical, Meyer's interpretation must be erroneous, for in the H.R.l. the mass lies caudal to Hensen's node.

The ventral surface of the streak proper is finely irregular and shows no trace of the presence of a basement membrane. Ventral to it the entodermal roof of the yolk-sac is intact.

Owing to the section plane it is impossible to be certain whether the edges of the streak proper are actively giving rise to intra-embryonic mesoderm or not. The subject will be dealt with later, when the intra-embryonic mesoderm is considered.

THE HEAD PROCESS.

A short mass of cells, broader at its caudal end than at its cranial end, has been identified as the primordium of the head process in H.R.l. The mass is clearly in continuity with the cranial end of Hensen's node and its nuclei are identical, both in staining reactions and in appearance, with the nuclei of the node. It is not more than .04 mm long and is

therefore in an early stage of development. Except near its cranial end, which is difficult to determine precisely, the cells of the process are columnar and present a picture (fig.26) which suggests that they might in reality be entodermal. That possibility, however, is excluded by the continuity of the process with Hensen's node and by the character of its nuclei. Further, within the cavity of the yolk-sac in this region there are five desquamated entodermal cells (one each in 19.7, 19.8 and 19.10 and two in 19.11) in addition to some detritus in 19.12 which may represent the remains of one or two entodermal cells. It is suggested that these are some of the cells which originally formed the roof of the yolk-sac in this situation and which have been replaced by the cells of the head process. In this connexion it should be observed that in the Embryo Fetzer, which shows no sign of a head process, the cells in the median plane of the yolk-sac roof immediately cranial to the primitive streak are vesiculous in character.

Apart from the Embryo Meyer, which has already been discussed and excluded (p.31/32), the H.Schm.10, the Hugo and the Bi.24 are the youngest which show the presence of an undoubted head process. In H.Schm.10 a head process, .1 mm long, is already present and in one section it contains a space, lined dorsally by high columnar epithelium and ventrally by low columnar epithelium, which is identified by Grosser (1931) as Lieberkühn's canal. In the Hugo the head process is .09 mm long and consists of an irregularly defined mass of mesodermal cells, more compact at its caudal end than at its cranial end.

The cells of which it consists are in continuity with the intra-embryonic mesoderm on each side and with Hensen's node caudally; they are fusiform or rounded in shape for the most part, but nowhere are they columnar. In no human embryo yet described, with the exception of Grosser's H.Schm.10, have any columnar cells been observed in the head process. According to Stieve the head process of the Embryo Hugo has no entoderm on its ventral surface, but Florian believes that the entodermal roof of the yolk-sac is intact. I am satisfied that the structure in question in H.R.1. is a derivative of Hensen's node, but it will be necessary to wait until other embryos of the same stage are available before one can be certain that it is the normal, early condition of the head process.

The cloacal membrane will be described with the entoderm (p.41).

THE YOLK-SAC.

Attention has already been drawn to the small size of the yolk-sac and this feature can be appreciated better from a consideration of the Table on page 66a. The reasons why it is masked in the reconstruction model and in the actual sections has been explained earlier in this thesis (p.5). Too much stress should not be laid on the size of the yolk-sac as an indication of normal development, for although there is naturally a distinct tendency for the yolk-sac to enlarge proportionately to the growth of the shield prior to the appearance of the head- and tail-folds, there are many notable exceptions.

The entoderm lining the yolk-sac is remarkably varied in its structure. The roof, apart from the region of the prochordal plate and the head process, is formed of flattened cells and low, cubical epithelium. The ventral wall of the sac shows the widest range of variation. At one point (fig.41) there is a small patch of five or six typical, high columnar cells. A large area is covered by low columnar epithelium, including some very large and obviously degenerating cells with spherical nuclei, some of which are hydropic and others intensely pycnotic. Low columnar epithelium covers the ventral wall of the caudal diverticulum in the neighbourhood of the origin of the allantoic cord (fig.11). Elsewhere the cells are elongated and somewhat flattened. In patches these cells are almost endothelial in their appearance; often they form what has already been termed a "syncytial ribbon". That the last two varieties are different forms of the same type is shown by their repeated occurrence in immediately adjoining areas, and by the fact that where the 'endothelial' type occurs the cytoplasm is obviously coagulated and shrunken. The same two types of epithelium are found in adjoining patches in the Strahl-Beneke Embryo, and are present, though not so conspicuous, in the Embryo Hugo. The 'syncytial ribbon' type appears to be better fixed than the 'endothelial' type.

In all embryos the ventral wall of the yolk-sac shows the greatest range of variation as regards the number and the character of the cells.

In view of the varieties of epithelium to which the

intraembryonic entoderm gives origin in the course of development, the variations noted in H.R.1. are not altogether surprising. Nevertheless, it must be stated that the cells in the roof show less variation than the other walls, and this may prove to be of importance in connexion with (1) the view advanced by Corning (1925) and supported by Stieve (1936) on the evidence of the findings in the Embryo Werner; and (2) the view recently advocated by Streeter (1936). Corning's theory that the yolk-sac cavity is originally part of the magma cavity outlined in primary mesoderm and that the entoderm of the roof, which is derived from the inner cell mass, gradually spreads over the interior of the cavity, is neither confirmed nor refuted by the evidence from H.R.1. The possession of an obvious variety of potencies in the cells of the ventral wall of the yolk-sac might, on the other hand, be regarded as evidence in favour of Streeter's view (already stated, p.29), in accordance with which differences in the characters of the roof and the other walls of the yolk-sac might be anticipated. It must, however, be emphasised that at this stage the potencies of the cells concerned are apparently not yet materially reduced and the exhibition of different tendencies in different areas does not of itself necessarily imply differences in developmental origin. I regard the fact, that the "syncytial ribbons" are found (1) in the roof of the amnion, (2) in the walls of the precocious coelomic cavity and (3) in the wall of the yolk-sac, as evidence that the differentiation of the ecto-, ento- and mesoderm has not yet affected seriously the potencies of the

cells concerned.

THE ALLANTOIC CORD.

The condition of the allantoic representative in the H.R.1. calls for further consideration. It is a solid cord of entoderm which - due allowance being made for the kink in the connecting stalk - arises in the median plane from the apex of a funnel-shaped diverticulum from the caudal wall of the yolk-sac. It passes at once into the connecting stalk and measure .135 mm from base to tip. At its distal end it takes part in the formation of the cloacal membrane over an area .1 mm long.

The early history of the allantois in the human embryo is still very obscure. In the Bi.24 (Florian, 1931), which is at a slightly later stage of development than the Hugo, an allantoic canal is present, measures .13 mm in length, and takes a large share in the formation of the cloacal membrane. In all older embryos it is present as a patent, tubular diverticulum. It measures .19 mm in the Manchester Embryo (Hill and Florian, 1935), .14 mm in the Thompson-Brash (1923), and .21 in the Peh.1 - Hochstetter (Rossenbeck, 1923). Its relationship to the cloacal membrane in these older embryos is variable. In the Manchester, the Dobbin (Hill and Florian, 1931) and the Thompson Brash it takes no part in the formation of the membrane, whereas in the Peh.1 - Hochstetter and Grosser's Embryos Kl.3 (1913) and Wa.17 (1931) it forms a large part of it.

In the Ingalls Embryo (1918) there is a small area of ecto-entodermal connexion involving the allantois and separated

by a gap from the cloacal membrane proper.

In the Embryo Hugo, according to Stieve's (1926) description, "ist kein deutlicher Allantoisgang oder eine Allantoisbucht vorhanden". A very small recess in the dorsal part of the caudal wall of the yolk-sac is tentatively regarded as the allantoic representative.

In embryos at an earlier stage of development than the H.R.1. the condition of the allantoic representative has given rise to considerable discussion. Grosser (1913) identified an allantoic diverticulum in the Embryo Peters, and von Möllendorff originally described a large diverticulum of the yolk-sac in the Embryo O.P. as the allantois, but in both these embryos it is now generally agreed that no allantoic representative is present. In the Embryo W.O., which is slightly older than the O.P., a solid mass of thickened entoderm projects dorsally from the roof of the yolk-sac at the caudal end of the embryonic area. Von Möllendorff (1925) regards this as the primordium of the allantois, and put forward the view that in the human embryo the allantois arises as a solid outgrowth which acquires a lumen later. Florian (1929) opposes this view and regards the entodermal outgrowth as the primordium of the cloacal membrane, which he has identified in the Embryos Fetzer and Bi.1. In the figures already published of Bi.1 (the full description has not yet appeared) the allantois is represented by a solid entodermal outgrowth with a small central cavity, which projects from the caudal wall of the yolk-sac and fuses with the ectoderm over a small area. Florian,

however, is now of opinion that this structure is not the definitive allantois but is destined to become incorporated in the yolk-sac and to be replaced by the true allantois at a later stage. In the Embryo Fetzer no trace of any allantoic representative is present.

The condition in the Strahl-Beneke Embryo furnishes a close parallel to the condition in H.R.1. The yolk-sac, which is slightly distorted, gives off an irregularly shaped recess at the junction of its roof with its caudal wall. This recess may in reality be due to the distortion, but it seems to represent the funnel-shaped caudal recess present in H.R.1. From its summit a solid entodermal cord passes into the connecting stalk and comes into continuity near its distal end with the ectoderm of the amnion. It measures .09 mm long. In the Embryo T.F. the allantois is, doubtfully in my opinion, represented by a small diverticulum from the dorsal end of the caudal wall of the yolk-sac, so that the condition is not dissimilar to the condition of the Embryo Hugo. In the Embryo Meyer a funnel-shaped diverticulum projects dorsally from the caudal end of the yolk-sac roof into the connecting stalk. The end of the diverticulum is formed by a short, solid mass of entoderm, which may possibly be more extensive than is represented in Meyer's figures. Florian (1929) is of opinion that a cloacal membrane is probably present in connexion with the allantoic outgrowth, which measures not less than .12 mm in length. In Grosser's Embryo H.Schm.10 (1931) the allantois is represented by a tubular diverticulum with relatively thick

walls and a very narrow lumen. It is .05 mm long and in the neighbourhood of its solid tip its epithelium is fused with the amniotic covering of the connecting stalk.

From this evidence it is possible to draw some tentative conclusions with reference to the early development of the allantois. The Embryos W.O., Bi.1, Strahl-Beneke, H.R.1, Meyer and H.Schm.10 form a series which suggest that the primordium of the allantois is a solid entodermal cord which establishes continuity with the ectoderm of the amnion covering the connecting stalk at an early stage. It acquires its lumen later, probably as an extension of the yolk-sac cavity into the cord. On the other hand, the conditions found in the Embryo Hugo and the Embryo T.F. make it clear that the actual time of appearance of the allantoic representative is subject to considerable variation. If the small diverticula from the yolk-sac in both embryos are accepted as representing the allantois, only two alternative explanations are possible. (1) The allantoic representative appears as a solid cord which soon becomes atrophied and disappears, its proximal end forming the site of the hollow allantoic canal. (2) The allantois may develop either as a solid entodermal rod, or as a small, hollow diverticulum which rapidly enlarges and grows into the connecting stalk. On the whole it seems more probable that the development of the allantoic primordium has been delayed in both cases, and that the identification of the small diverticula as allantoic representatives is not justified. The question, however, is complicated by the relationships exhibited by the cloacal membrane.

THE CLOACAL MEMBRANE.

This remarkable structure has been very fully investigated by Florian, who has succeeded in identifying it in embryos as early as the Fetzer and the Bi.1. Further he believes that it is probably present in the Embryo W.O. One therefore anticipated confidently that a cloacal membrane would be present in the H.R.1., but no connexion could be observed between the roof of the yolk-sac and the shield ectoderm. Professor Florian, with whom I was in correspondence, suggested to me that it might be found caudal to the shield, and he proved to be right. In the H.R.1. (figs. 22 and 24) the cloacal membrane is associated with the terminal .1 mm of the allantoic cord and extends between it and the amniotic covering of the connecting stalk immediately caudal to the shield. It is cut obliquely but its identification is unequivocal in sections 19.7 and 19.8, though it is not quite so convincing in sections 19.6, 19.9 and 19.10. The ectodermal cells of the most dorsal part of the membrane (upper part in the figures) were mistaken at first for a large blood island, but further examination demonstrated their continuity with the cells of the allantoic cord and with the cells lying ventral to them (below, in the figures). These cells contain a few of the darkly staining droplets which have been mentioned in connexion with the shield ectoderm (p.27). It is important to observe that in the Strahl-Beneke Embryo also the ectoderm concerned in the formation of the cloacal membrane is amniotic. On the other hand, both in the Bi.1 and the Fetzer Florian has identified the membrane within the limits of the

shield and in the Bi.24 it is situated partly in the shield and partly in the connecting stalk. In older embryos it is situated either wholly within the shield (Thompson-Brash, Manchester, Dobbin, etc.) or it may involve both the caudal end of the shield and the adjoining amniotic ectoderm of the connecting stalk (Peh.1 - Hochstetter, Sternberg (1927), Grosser's Kl.13, etc.).

The question at once arises as to whether the cloacal membrane in H.R.1. and the Strahl-Beneke is identical with the structure described by Florian in the Fetzer (1930) and the Hugo. In both the H.R.1. and the Strahl-Beneke the cloacal membrane is outside the shield area and involves the allantoic cord only. In the Fetzer it lies within the limits of the shield and involves the roof of the yolk-sac - (the allantois is not yet present). It may be, as Wyburn (1937) appears to believe, that the cloacal membrane in the Fetzer indicates the site at which the allantois will subsequently develop, but Florian in his Figures 1a and 1b places it definitely within the area of the shield. If the two structures are identical it follows that, in order to account for the conditions found in the older embryos, the cloacal membrane may appear either in the connecting stalk and later extend cranially on to the shield, or in the shield and later extend caudally on to the stalk. That such a variability in the origin and growth of the cloacal membrane should occur is extremely improbable, and one is forced to the conclusion that if Florian's identification of the membrane in the Embryo Fetzer is justified, the two structures cannot be identical. It would then be necessary, in order to

explain the ecto-entodermal fusion in the Strahl-Beneke and the H.R.1., to fall back on the possible occurrence of a "canalis amnio-allantoideus". This structure was described by Schauinsland (1902) in Lacerta and was called in by Ingalls to explain a very small area of amnio-allantoic fusion(1918). Schauinsland's description is far from convincing for Lacerta and there is no evidence available to justify the suggestion that the rudiments of such a structure are normally present in the human embryo, and the fact that amnio-allantoic fusion is present in the Strahl-Beneke, the H.R.1. and the H.Schm.10 is sufficient to show that the fusion is a normal feature. In discussing Grosser's H.Schm.10, Florian (1933) makes it clear that he regards ecto-entodermal fusion and not contact as the criterion for the recognition of the cloacal membrane. He rejects an area of contact at the caudal end of the primitive streak within the shield area and accepts the amnio-allantoic fusion in the connecting stalk as the cloacal membrane. In this way he brings the H.Schm.10 into alignment with the Strahl-Beneke and the H.R.1.

The whole question, however, bristles with difficulties and can only be solved when further material has become available. Meantime, I incline to the view that the cloacal membrane develops later than the allantois and in close association with it, and at a later period extends into the caudal end of the shield. This is a modification of the view recently put forward by Wyburn (1937) who, however, had access to no material younger than the McIntyre 1, which has well-

developed head- and tail-folds and measures 1.4 mm.

THE PROCHORDAL PLATE.

The patch of thickened entoderm which forms such a conspicuous feature in the roof of the yolk-sac in sections 19.9 - 20.3 has already been identified as the primordium of the prochordal plate. It measures .075 mm long x .05 mm wide and its cranial limit lies .12 mm from the cranial border of the shield. Except towards its right margin it is connected to the basement membrane of the shield ectoderm over an area which varies in extent from section to section. It is certain that the connexion was both real and extensive, probably considerably greater than is represented in the median section of the model, (fig.31). In most of the sections in which it is cut the plate consists of from ten to twelve large, vesiculous cells, with large round or oval nuclei and with only suggestions of cell boundaries. The cytoplasm is lightly staining and contains many vacuoles. The ventral surface of the plate is covered with the fine coagulum content of the yolk-sac (fig.31), and at its caudal end it is uncertain whether or not the plate is continuous with the cranial end of the head process, although the continuity, if it exists, is exceedingly tenuous.

Florian (1930) has described and figured a patch of similar cells in the roof of the yolk-sac in the Embryo Fetzer, but in this case the cells form a single layer and lie immediately cranial to the primitive streak. A corresponding patch of thickened entoderm is present in the Strahl-Beneke and

its position and the characters of its constituent cells indicate quite clearly that we are here dealing with the same structure as is present in H.R.1. In the Embryo Hugo, on the other hand, Stieve (1926) makes no mention of the existence of any corresponding structure although his figures 12 and 13 are rather suggestive, and in the H.Schm.10 Grosser (1931) says "Eine Prächordalplatte lässt sich nicht mit Sicherheit nachweisen".

In the Bi.24 and older embryos the prochordal plate is a constant structure.

The prochordal plate in the Strahl-Beneke and the H.R.1 might conceivably have another interpretation. The vesiculous character of the cells concerned might be regarded as a degenerative change prior to desquamation to provide space for the growing head-process. On the other hand, the nuclei are healthy and active in appearance, and desquamation does not necessitate a prior thickening.

Attention should be drawn to the adhesion of the plate to the basement membrane of the shield ectoderm, and to the relation existing between the plate and the precocious coelomic cavity. Both point to the possibility of a relationship between the prochordal plate and the buccopharyngeal membrane.

CONTENTS.

The yolk-sac contains in places a small amount of very lightly staining and foam-like coagulum which, although situated centrally for the most part, is also present in many

sections in contact with the roof and the caudal wall. It is seen in fig.31 in close relation to the prochordal plate. The presence of such a coagulum in the yolk-sac has been noted by many observers and may indicate secretory activity of the entoderm or it may be the result of post-mortem changes. In addition the yolk-sac contains a few desquamated entodermal cells, especially in the region of the head-process as already stated.

ENTODERM CYSTS.

A careful search was made for isolated entodermal cysts in the chorionic cavity, although the fact that the specimen had been reblocked after the cavity had been opened implied that a negative result would not necessarily mean that none had been present originally.

In 7.2 - 9.2 a patch of undoubted entodermal cells was discovered which had become entangled in a film of coagulum. It comprises 4 - 10 cells in each section. The nuclei are rounded or oval, lightly staining but well fixed. Although the cells are in many instances vesiculous in appearance, they form a solid clump with no sign of cavity formation.

THE INTRA-EMBRYONIC MESODERM.

Except in the region of the median plane caudal to the prochordal plate, the intra-embryonic mesoderm forms a continuous open meshwork over the whole of the embryonic area.

Round the periphery of the shield the cells are not very numerous but they are connected to one another by branching processes. Wherever they reach the periphery of the shield they become continuous with the primary mesoderm and at the caudal end they pass into the connecting stalk. In places the mesoderm cells fill up the whole interval between the ectoderm and the entoderm, but as a general rule shrinkage spaces intervene between the mesoderm and one or both of the two other layers. In many situations the mesoderm cells appear to be springing directly from the deep surface of the shield ectoderm and elsewhere they are often connected to it by fine cytodesmata; in other situations they are intimately related to and apparently continuous with the entoderm of the roof of the yolk-sac. There is no evidence to show whether these cells are actually derived from the primitive streak, the primary mesoderm, the shield ectoderm or the entoderm. Stieve (1926) believes that the intra-embryonic mesoderm at this stage is derived (1) from the primary mesoderm (2) from the primitive streak and (3) from the entoderm of the roof of the yolk-sac. The histological appearances, however, may be very misleading and I am of opinion that the Embryo H.R.1. provides no definite evidence in this connexion.

Typical mesoderm cells can be seen in figs.26 and 27 apparently arising from the caudal surface of Hensen's node, and others are seen in figs 24 and 25, apparently arising from the cranial surface of the node and lying dorsal to the left edge of the head process.

To the right of the median plane the sections become more oblique owing to the curvature of the shield. Two consecutive sections pass between the right wall of the yolk-sac and the shield ectoderm (fig.37). In these the fusiform cells of the intra-embryonic mesoderm form a continuous open-meshed network from the cranial to the caudal periphery of the embryonic area by means of their interconnected branching processes.

In sections 18.9 to 19.3 (figs. 11 - 17) the exocoelom encroaches on the embryonic area at the cranial end of the shield and the primary mesoderm which lines the invagination is directly continuous with the intraembryonic mesoderm, so that it is impossible to be certain where the one ends and the other begins. In the two succeeding sections the intraembryonic mesoderm at the cranial end of the shield contains a cavity which appears to be shut off from the exocoelom, which no longer encroaches on the embryonic area (cf. figs 13 and 19). In the nine succeeding sections the same cavity is present, although it is partly interrupted in 19.8 and is damaged in 19.11, and it extends cranially practically to the limit of the shield. This cavity-containing mesoderm extends caudally to the region of the prochordal plate.

Only two possible interpretations can be suggested for this cavity, for the appearances exclude the possibility of vascular formation. Either it is an artefact due to shrinkage, or it is a precociously developing coelomic space. At first sight the former explanation is the more probable. No trace

of any such cavity is present in other embryos at this stage.* In the Dobbin Embryo (Hill and Florian, 1931) which is .96 mm long, the minute cavities apparent in two of the sections are regarded by the authors as very doubtful coelomic formations. On the other hand the appearances in H.R.1 are strongly suggestive of coelomic formation. The continuity of the cavity through so many sections alone throws grave doubt on the likelihood that we are here dealing with an artefact. In some of the sections cytodesmata connect the dorsal wall to the shield ectoderm, but no cytodesmata are found within the cavity. In two of the sections (19.12 and 20.1, figs 29 and 32) the walls of the cavity present the 'syncytial ribbon' appearance which has already been shown to be indicative of good fixation and preservation. One is therefore forced to conclude that the cavity is a natural space within the intra-embryonic mesenchyme and as such it can only represent a precociously developed coelomic space.

* In the embryo described by Schlagenhaufer and Verocay (1916), which is only .24 mm long, mention is made of a cleft in the intra-embryonic mesoderm near the cranial end of the shield. The cleft appeared in one section only and was not figured. As the description is very incomplete it is impossible, without examining the sections, to come to any conclusions about it. It is regarded by the authors as suggestive of a coelomic formation.

THE PRIMARY MESODERM.

On the amnion the primary mesoderm forms a single layer of cells, except around the periphery of the embryonic shield where it forms a rather thicker layer on the up-turned rim. Towards the cranial and caudal limits of the amniotic roof no difficulty is experienced in distinguishing the mesodermal from the ectodermal layer. The mesodermal cells are fusiform with prominent nuclei: the ectodermal cells also are elongated but their nuclei do not project above the general level. Over the central part of the roof the two layers are indistinguishable and in the sections they form a ribbon-like syncytium (fig.26). The same appearance has already been noted in the wall of the coelomic space and in the wall of the yolk-sac. In the latter situation and in the amniotic roof similar areas are present in both the Strahl-Beneke and the Hugo Embryos. The condition has been discussed at an earlier stage (p.35).

On the yolk-sac two types of cells can be identified without difficulty. The first type, which greatly exceeds the second in number, comprises cells which are almost epithelioid. Their nuclei are rounded and relatively large; they do not stain darkly but their nucleoli are conspicuous and they contain a fine chromatin network. In some places the cells of this type form a single layer, but in many others they form clumps of variable size, containing from five to thirty cells. The second type comprises a number of elongated, flattened cells. They are found in places covering the entoderm but they are more commonly situated amongst the clumps of cells of the

first type, where they help to form the walls of intercellular spaces.

These clumps are regarded as blood islands and the occasional spaces as early stages in the formation of vascular spaces. In the islands the cell boundaries are indistinct and the cytoplasm is pinkish in tint. The vascular spaces are neither so large nor so numerous as those found in the same situation in the Embryo Hugo; they are all small in size and they do not communicate with one another.

The Connecting Stalk extends from the apical part of the chorionic vesicle to the caudal end of the embryonic area and the adjoining part of the roof of the amnion. Attention has already been drawn to the gap which is apparent between the connecting stalk and the dorsal surface of the funnel-shaped diverticulum from the caudal surface of the yolk-sac (figs. 19 etc.). Although, as stated, the gap is regarded as a tear in the embryonic attachment of the connecting stalk, the appearances of its boundaries would lead one to suppose that it is a natural interval, and the evidence in favour of the interpretation put forward is mainly of a negative character. If it is not a tear, then the connecting stalk has a very narrow attachment to the embryo and a very wide attachment to the amnion, a condition which is not impossible but which is exceedingly improbable. The allantoic cord has a pronounced bend towards the left and its connexion with the yolk-sac has been displaced considerably to the left of the median plane.

Such a condition can be explained satisfactorily by a tear of the connecting stalk, as already indicated. Finally, no corresponding gap is present in other early human embryos.

The ab-amniotic surface of the stalk is covered with loosely arranged and loosely connected epithelioid cells which occasionally form small surface clumps very similar to the blood islands on the yolk-sac. As the stalk is traced towards its chorionic attachment it becomes less cellular and is looser in texture. Actual spaces - which are rare in the vicinity of the embryo apart from contraction spaces - are more numerous and are relatively large, much larger than the spaces in the wall of the yolk-sac. Many of them are surrounded by flattened cells which indicate their vascular character (fig.42).

As already stated, the connecting stalk contains the allantoic cord and the whole extent of the cloacal membrane.

THE CHORION.

The fixation and preservation of the constituent parts of the chorion are not unnaturally still better than the fixation and preservation of the embryo itself.

The primary mesenchyme which lines the chorion and extends into the chorionic villi and their branches is everywhere closely applied to the cytotrophoblast. As will be seen from fig.2, no shrinkage has occurred and in this respect the tissues are as well preserved as they are in the Strahl-Beneke and the Hugo Embryos.

The constituent cells of the mesenchyme exhibit many variations in form but the majority are elongated and lie with their long axes parallel to the cytotrophoblast both in the chorionic wall and in the interior of the villi. (1) Fusiform cells with branching processes at each end are very numerous (fig.43). They tend to occur in short strings of two or three, especially in the villi. Their nuclear structure is distinct; the nucleolus is prominent and the chromatin network is clearly shown, although it is not darkly stained. (2) Elongated, rod-like forms are also numerous. Their nuclei stain so darkly that their structure cannot be made out. These cells also tend to occur in short strings which suggest the angioblastic strands described by Maclaren. (3) Smaller, rounded cells with deeply staining nuclei and scanty cytoplasm form a less numerous group. (4) In addition, short rod-like forms occur with deeply stained nuclei. They may be the earlier stages of group (2), or they may be cells of group (2) which have been cut obliquely to their long axes. (5) Within the villi, and in places in the chorionic wall, large mesoblasts with oval nuclei and branching protoplasmic processes are common (fig.43). Their nuclear structure is clearly shown and they appear to represent early stages of the cells in group (1).

No indubitably vascular spaces and no blood islands are present in any part of the chorion, although angioblastic strands, of somewhat doubtful identity, were recognised in the apical region of the chorion. Hertig (1935) has recently put

forward the view that both mesoblasts and angioblasts are direct derivatives of the cells of the cytotrophoblast and claims to have recognised angioblastic strands in the mesenchyme of the Miller ovum. If his interpretation is correct, it is strange that no obvious angioblastic tissue can be identified in the chorionic mesenchyme of H.R.1. and that such as is present has not developed in the interval between the two stages, for the H.R.1 is certainly at least two and not improbably three or even four days older than the Miller ovum. At the same time it must be remembered that the H.R.1 required to be reblocked after the chorionic cavity had been opened and it is possible that in the process the superficial parts of the chorionic mesenchyme might have suffered injury or loss. In this way the absence of the mesothelial layer, which MacIntyre has described as present in T.B.2, may be accounted for, because it is only in a few places that cells are present which are worthy of the name 'mesothelial'.

The Chorionic Villi cover the whole of the outer surface of the chorion. They are longest and most crowded together in the region of the decidua basalis (fig.2), where they average 0.6 mm in length. In this situation they show fewer branches than they show in the lateral walls of the chorion, where they tend to be both broader and shorter. Being more widely spaced they are able to branch freely and as many as 10 - 12 branches may arise from one villus (fig.44). In the region of the decidua capsularis the villi are shortest

and measure on the average 0.2 mm. They are narrower than the villi in the lateral walls and show fewer branches.

The cells of the mesodermal cores of the villi are especially well preserved and show numerous branching and anastomosing processes. Fusiform cells predominate and arrange themselves in the long axis of the villus or its branches. They have been described on p.53.

The Cytotrophoblast forms an easily recognisable layer over the whole surface of the chorion and the chorionic villi. The cells are regularly arranged and show little variation in size. It is a curious fact that although most of them possess nuclei with a clearly defined chromatin network, many of them exhibit darkly staining pycnotic nuclei in which no trace of structure can be discerned.

From the apices of the villi typical cell-columns are continued into the trophoblast shell which forms the outer boundary of the intervillous space. The cells in these columns vary considerably in size. The smaller cells are found at the apices of the villi, where they are closely crowded together. The larger cells are found in the trophoblast shell and show large intracellular shrinkage spaces (fig.45). In addition the chromatin network of the nuclei is irregularly disposed and appears to have undergone shrinkage in many places, leaving clear areas which are unstained. The appearance indicates that many of these cells are undergoing degenerative changes. It is certain that at the apices of the villi the cell columns are

actively growing and it is a curious fact that in nearly 400 sections only a few, very doubtful mitotic figures were seen. Florian (1928) has suggested that the nuclei in the plasmodium increase by amitosis, and the absence of mitotic figures strongly suggests that the same process is the normal method of cell-division in the cytotrophoblast.

THE PLASMODIAL TROPHOBLAST.

The cytotrophoblast of the chorionic membrane and of the chorionic villi is everywhere covered with a thin layer of plasmodium to which Florian (1928) has given the term resorption-plasmodium. It is this layer which is bathed by the maternal blood in the intervillous space and through which all the nutritive substances must pass before they can reach the embryo.

The plasmodium has the appearance of a very fine foam, and its free surface shows the well-recognised "brush border". The contained nuclei are irregularly spaced, and tend to be flattened against the cytotrophoblast. For the most part they are darkly staining and their structure is difficult to discern. No mitotic figures were seen, but on the other hand, no dumbbell forms, such as Florian has described, were encountered.

The cytotrophoblast of the cell columns is covered for the most part with plasmodium, but there are many patches where no covering plasmodium is visible and the chorionic

surface of the cytotrophoblastic shell is in direct contact with the maternal blood of the intervillous space.

Islands of free plasmodium are found in the intervillous space. They are usually pale in colour; the fine foam has become coarser in character and contains numerous vacuoles; and the contained nuclei show obvious retrogressive changes. In many of these islands the nuclei are dark and pycnotic and have lost their regular outline; in others the nuclei are swollen and hydropic, are pale in colour and contain only a nucleolus and some shrunken shreds of chromatin. They are obviously in process of dissolution. Although they occur generally throughout the intervillous space, they are few in number under the decidua basalis and numerous under the decidua capsularis.

Areas of healthy-looking plasmodium occur in the midst of the trophoblastic shell and around the periphery of the shell in contact with the endometrium. Many of these areas line slit-like spaces in the shell (fig.46), but others appear to be surrounded completely by the cytotrophoblast. Where a free surface presents itself for examination the 'brush border', which is so characteristic of the 'resorption plasmodium', is absent or inconspicuous. Florian (1928) has termed this the 'proliferative plasmodium', as he believes that it differs materially in its function from the 'resorptive plasmodium'.

Both in the trophoblast shell and in the peripheral zone the strands of proliferative plasmodium are easily recognised on account of their distinctive staining reactions. The nuclei stain so darkly with haematoxylin that their structure

can be made out only with difficulty, while the surrounding plasmodium stains reddish pink with eosin. In the peripheral zone, particularly, the nuclei are elongated, being fusiform or rodlike, and the associated plasmodium is drawn out into strands in the long axis of the nucleus. Some of these strands contain three or four nuclei end to end and they are actively streaming into the endometrium (fig.45). In the maternal tissues they are found at considerable distances from the trophoblast shell. In these situations it is exceedingly difficult to convince oneself that they form part of an open-meshed plasmodial network and not independent cells. The units can be seen in contact with the walls of the maternal blood-vessels, and uterine glands, and the adjoining maternal cells present the appearances of incipient degenerative changes. Occasionally the nuclei of these plasmodial strands are V- or Y-shaped, and in places they lose their elongated shape and become irregularly quadrangular. In the latter case the surrounding plasmodium adapts itself to the altered shape of the nucleus. In many situations one strip of plasmodium contains two elongated nuclei lying side by side, and these forms, together with the V- and Y-shaped nuclei, give support to Florian's view that in the plasmodial trophoblast amitotic nuclear division is the rule. The Y-shaped nuclei represent the first stage, the V-shaped nuclei the second, and the side-by-side nuclei the third and completed phase of the process.

The proliferative plasmodium can be seen in close relationship with the uterine vessels, which it is presumably

attacking. The walls of the arterioles concerned are thickened and their lining endothelial cells are swollen. In many places the proliferative plasmodium has replaced the endothelium lining the wide venous sinuses which surround the ovum, and in these situations its margin is always clear cut and no 'brush borders' are apparent.

Within the trophoblastic shell there are numerous straight channels which are parallel to the veins in the adjoining part of the stratum spongiosum. They are lined for the most part by the proliferative plasmodium (fig.46) but here and there small patches retain a lining of endothelium. These spaces and the presence of proliferative plasmodium in the walls of the venous sinuses immediately outside the trophoblastic shell suggest that, after the implantation of the ovum, the implantation cavity is enlarged, in part at least, by the incorporation of the adjoining venous sinuses. The mechanism of the process would appear to be the following. Strands of proliferative plasmodium attack the walls of the vessel, destroy and replace the lining endothelium. The trophoblastic shell enlarges at the expense of the intervening maternal tissues until the sinus becomes separated from the intervillous space only by the proliferative plasmodium and the trophoblastic shell. Degenerative changes occur in the trophoblast so that new spaces are formed which enable the sinus to communicate with the intervillous space. A new trophoblastic shell is then formed on the opposite side of the sinus which gradually loses its identity, becoming merged eventually in the intervillous space.

THE ENDOMETRIUM.

The uterine mucosa presents the typical appearances associated with an early pregnancy. The compact and spongy layers are quite characteristic (figs 2 and 3).

The glands of the stratum spongiosum are enormously dilated and full of secretion, and in the vicinity of the ovum some contain extravasated blood. The lining epithelium displays the "saw-teeth" appearance, except in the immediate neighbourhood of the ovum where the walls of the glands are much less irregular than they are elsewhere (fig.47). Presumably these glands have been subjected to considerable internal pressure for their lining epithelium is flattened in many places and in some situations is awanting.

The functional meaning of this excessive glandular enlargement has been discussed recently by Falkiner (1932). Like many other writers he accepts the view that the secretion of the uterine glands provides nourishment for the ovum after it reaches the uterine cavity and prior to implantation. It is, however, a commonplace that in tubal gestations the ovum may develop and form a normal embryo, although it is then unable to benefit by the secretion of the uterine glands. Again, the degree of dilatation and the amount of the secretion is out of all proportion to the amount of nourishment required by the ovum. It is clear therefore that the production of 'embryotrophe' is not only not the principal function of the glandular activity but that it is very doubtful indeed whether the ovum derives any nourishment from this source. In addition

to the function of producing 'embryotrophe' Falkiner ascribes to the glandular enlargement certain mechanical functions. He believes that it exerts "a definite effect on the blood-supply at the commencement of pregnancy, favouring the formation of a venous sinus". With this view the appearances in the stratum spongiosum of the H.R.1 are in complete agreement. The compression exerted by the enlarged glands in the immediate vicinity of the ovum on the venous return from the area is seen in a large number of the sections, and undoubtedly helps to determine the character of the circulation in the intervillous space, which will be considered later in this section. In addition, Falkiner ascribes to the glandular enlargement the function (1) of forming a layer impervious to the action of the trophoblast, (2) of providing a natural line of cleavage, and (3) of providing a layer from which the mucous membrane may be regenerated post partum. That the glandular epithelium is very resistant to the destructive action of the proliferative trophoblast can be inferred from the appearances in numerous sections of the H.R.1. In many situations, ducts, surrounded by a small amount of stroma, are almost isolated by the trophoblast from the rest of the endometrium. Where 'peninsulas' of the mucosa occur, they almost invariably contain ducts.

The stratum compactum is infiltrated with a large number of small round cells which are obviously lymphocytes. No typical decidual cells are present. Small areas of localised oedema, which tend to spread into the more superficial parts of the stratum spongiosum, are a prominent feature. In many

situations these areas are traversed by small veins which contain a disproportionately large number of white blood corpuscles (fig.48). A similar condition has been noted in the endometrium by Stieve, Falkiner and many other observers. Sandison (1932) has shown that white blood corpuscles may occur in unusually large numbers in "any uncontracted blood vessel in which the circulation has temporarily ceased, but which remains connected with other circulating vessels". This phenomenon is therefore associated with extremely sluggish circulation and attention must be drawn to the evidence of such a type of circulation in the immediate neighbourhood of the ovum.

Large, thin-walled, venous sinuses are found in all young human ova closely adjoining the implantation cavity. They communicate freely with the intervillous space; they communicate with one another; and they are drained by a number of very large veins. One of these sinuses is shown in fig.50. It is placed deep to the decidua basalis and three veins are shown leading from it into the deeper layers of the stratum spongiosum. Falkiner (1932) has suggested that these sinuses owe their origin to the pressure of the dilated glands on the neighbouring veins, and the appearances in the H.R.1. certainly support his view.

If now we turn to a consideration of the arteries in the stratum compactum, we find a very different picture. Barthelmez (1931) and Daron (1936) have shown that, apart from some minute branches which are restricted to the deepest part of the stratum spongiosum, all the arteries follow a very tortuous

course, so that the same vessel is cut in many places in the same section. This character makes the arteries easy to identify but difficult and tedious to trace. They run in the interglandular tissue surrounded by a sheath of stroma, whereas the veins run in close relation to the walls of the glands and have little or no surrounding stroma in the stratum spongiosum. In the vicinity of the trophoblast shell in the H.R.l. the tissue around the smaller arteries shows no signs of oedema (fig.48) as compared with the tissue around the smaller veins. The arterioles themselves are the subject of attack from the proliferative trophoblast and show resulting changes. Their walls are noticeably thickened and the thickening involves both the endothelial lining and the outer walls. Despite a very prolonged search I was unable to trace any of these arterioles into the intervillous space or into any of the venous sinuses. In many situations small branches of the arteries almost succeeded in reaching the intervillous space but their ends were always occluded and usually sealed off by fibrin. A similar fibrinous change was found in several of the larger arterioles in the stratum compactum in the immediate neighbourhood of the ovum (figs 50 and 51).

Although no arterioles were found opening into the intervillous space or the adjoining venous sinuses, a number of dilated capillaries were found in the decidua capsularis which undoubtedly established communications either directly or indirectly with the intervillous space. These capillaries contained the normal proportion of white to red cells and their

walls were not conspicuously thickened.

Falkiner succeeded in tracing one arteriole into one of the sinuses, and Stieve (1926) has figured a vessel, which he identifies as a small artery, opening indirectly into the intervillous space. He states further "Die Einmündung der Arterien in die weitiren Bluträume lässt sich an mehreren Stellen gut herbachten". Nevertheless he concludes that the circulation in the intervillous space and in the sinuses is exceedingly slow.

In the H.R.1. the blood in the intervillous space and the sinuses must have been almost stagnant. Only a relatively small number of capillaries could be traced into them so that the inlet must have been almost negligible. The sealing off of the small branches of the arteries seems to be a precaution to prevent a rapid circulation at this stage. Indeed, the areas of patchy oedema, the disproportionate number of leucocytes in the superficial and many of the deeper veins, the size of the venous sinuses, the sealing off of the arteries and the capillary type of inlet all point in the same direction. They indicate that, prior to the formation of blood vessels in the chorionic villi, and the establishment of the chorionic circulation, efficient nutrition of the embryo can only be ensured provided that the circulation in the intervillous space is so slow that the contained blood is practically stagnant.

One must not, however, overlook the fact that far more than adequate provision is made for the venous drainage

of the sinuses and the intervillous space. The presence of so many large and intercommunicating veins leading away from the immediate neighbourhood of the ovum suggests that the establishment of free circulation in the intervillous space at a later stage is not a gradual but rather a comparatively sudden process and ensures that increased entry of blood into the space, no matter how extensive, will not overtax the carrying capacity of the outlets.

The point of entry of the ovum was not identified. A large part of the decidua capsularis is covered by a substantial and comparatively recent blood-clot (fig.2). Where it is exposed on the surface it is covered by cubical epithelium, which, however, is not in a very good state of preservation. In its central part, where the point of entry probably was situated, a sheet of fibrinoid substance, staining well with eosin, forms nearly the whole thickness of the decidua. Its deep surface is covered, for the most part, with plasmodial trophoblast, but some shrinkage has apparently occurred in this region and has resulted in the separation of the trophoblast from the decidua. This sheet of fibrinoid substance is penetrated by strands of proliferative trophoblast and here and there contains broken down cells which are apparently duct epithelium and stroma cells. In the peripheral part of the decidua capsularis the stroma cells become more numerous but are still intermingled with strands of proliferative trophoblast. The remains of ducts are easily recognisable and

numerous dilated capillaries are present. The endothelial cells of these small vessels are slightly swollen and they are replaced in many situations by single units of the trophoblast. They contain a normal proportion of red blood corpuscles and many of them open into the venous sinuses or the intervillous space. In this part of the decidua capsularis small groups of lymphocytes are frequently to be observed.

In the peripheral zone it is not, as a rule, difficult to differentiate the foetal from the maternal tissues, although there is nowhere any necrotic zone such as is present in earlier stages, e.g., T.B.1 (Bryce, 1908) and von Möllendorff's Sch. (1921). Here and there fibrinoid patches are encountered and the maternal cells for the most part show signs of degenerative changes. The ducts appear to be least affected by the destructive process that is going on all around them and in many places are almost isolated by the trophoblast.

TABLE OF PRINCIPAL MEASUREMENTS OF THE HUMAN EMBRYOS TO WHICH SPECIAL REFERENCE IS MADE IN THE TEXT.

Embryo	Cavity of Chorion	Shield L.	Shield W.	Hensen's Node	Prim. Streak	Head Process	Cloacal Membrane	Allantois	Prochordal Plate	Cavity of yolk-sac	Villi Caps.	Villi Marg.	Villi Bas.
Fetzer	1.56 x 1.048	.26	.215		.05		+			.18 x .15 x .15	.18	.31	.14
Strahl-Beneke*	2.2 x 2.2 x 1.2	.37	.23		.1		+	.093	.066	.46 x .34			
Meyer	2.6 x 2.1 x 2.7	.41	.40		.12	.06?	?				.05		.2
T. F.	3.07 x 4.5 x 1.7	.4	.43		.162		+			.24 x .25 x .25	.18	.6	.45
H. Schm. 10		.51	.58	.1	.14	.1	+	.08ø		.9 x .7 x .45			
H. R. 1.	1.95 x 1.3 x 1.8+	.55	.43	.06	.115	.04	.1	.135	.075	.35 x .23 x .3	.2	.3-.6	.6
Hugo	4.4 x 4.7 x 3.8	.57	.63	.06	.24	.09	.035†	?	-	.52 x .64 x .53	.3		1.
Bi. 24	3.05 x 3.036 x 3.029	.62	.41	.05	.28	.1	.06	.15	.03				
Manchester		.87	.62	.05	.44	.12	.06	.21	.03	.98 x .74 x .98			

The measurements given are those published by the authors concerned except in the cases noted.

*All measurements as given by Florian, J. Anat. Anz. Erganz-zum Bd.71.

øMeasured by T.B.J. from the author's figure.

†Measured by Florian, J. Phil. Trans. Roy. Soc. London. Vol.219, Series B., p.480.

THE AGE OF THE EMBRYO.

The temptation to regard the dimensions of the embryonic shield as a reliable guide to the fertilisation age of the embryo has disappeared since Stieve (1926) published his description of the Embryo Hugo. In that case a period of only 13½ days elapsed between insemination and operation. If only 12 hours is allowed for the interval between insemination and fertilisation, the fertilisation age of the Embryo Hugo would be 13 days. In Bryce's Embryo T.B.1 (1908) the history was not less reliable than in the Embryo Hugo. An interval of 16½ days elapsed between insemination and the abortion. Bryce allowed 24 hours for the interval between insemination and fertilisation and a period of 24 - 36 hours between the death of the ovum and the actual abortion, and finally concluded that the fertilisation age of the embryo was 13 - 14 days. Thus 13 days may be regarded as the minimum for T.B.1 and as the maximum for the Embryo Hugo. But the developmental stage of T.B.1 is very considerably earlier than that of the Hugo, and according to Bryce's reckoning the latter would take its place in his series between the Leopold and the Reichert at an estimated age of 17 - 18 days.

Consideration of these two embryos makes it abundantly clear that the rate of development is by no means constant for human embryos and that two specimens of the same fertilisation age may differ in developmental stage by as much as 3 or 4 days. Such a disparity had been foreshadowed by Rabl (1915), who

showed that at 7 days 8 hours fertilisation age, rabbit embryos of the same litter might differ in shield length by as much as 50%.

In the embryo H.R.1 unfortunately no evidence is available as to the actual fertilisation age, but the developmental stage is clearly earlier than that of the Embryo Hugo and as clearly later than that of the Embryo Strahl-Beneke or the Embryo T.F. The operation of hysterectomy was performed on the day before the next period was expected to begin, or 27 days after the commencement of the last period. As the normal duration of the periods was 6 - 7 days, the maximum fertilisation age would be 19 days, if 24 hours are allowed as the interval between insemination and fertilisation. Assuming a developmental rate as rapid as that of the Embryo Hugo, the minimum fertilisation age would be in the neighbourhood of $12\frac{1}{2}$ days. The actual fertilisation age lies somewhere between these two extremes and is probably about $15\frac{1}{2}$ days.

Is the Embryo H.R.1. a normal embryo? This question must arise and deserves careful consideration in connexion with every young human embryo, and it is often exceedingly difficult to answer. Evidence is gradually accumulating to show that even the median plane structures are by no means constant in their relative times of appearance. This variability has been stressed by Grosser (1931) in two recent papers, and must be borne in mind when coming to a decision with regard to the Embryo H.R.1.

Our knowledge of the early stages of the human embryo is based on material obtained from one of three sources, viz:- (a) from operations, (b) from abortions, and (c) from post-mortem examinations. In groups (a) and (b) the condition of the endometrium must always be suspect, for, presumably, the specimens would not otherwise have been obtained. However, the condition of the endometrium in group (a) can always be examined, and in the H.R.1. it displayed no obviously pathological features. The specimens falling into group (c) may or may not be free from suspicion as regards the condition of the endometrium, but they nearly always give rise to doubts and difficulties because of their imperfect preservation due to the interval between the occurrence of death and the performance of the autopsy.

In H.R.1. the pronounced curvature of the shield, which has influenced the size of the yolk-sac, must be regarded as the result of an abnormal growth process (p.26). It may have been exaggerated during fixation, but probably not to any great extent. Does this abnormality of shape imply that no importance attaches to any of the features which it displays? Almost certainly not, for careful comparison with other embryos has shown that the median plane structures, with the exception of the coelomic cavity, are in a stage of development which are in harmony with the known facts and with one another. The primitive streak and its two nodes, the head process, the prochordal plate and the cloacal membrane can all be regarded as normal, with the possible exception of the head process

(p.34). The presence of a coelomic cavity must be regarded as evidence of precocity only, for it conforms in every way to the conditions which our knowledge of its normal development would have led us to anticipate.

To sum up, the Embryo H.R.1 is admittedly abnormal in shape and is precocious so far as coelomic development is concerned, but in other respects it is normal; and the evidence which it supplies in connexion with the development of the head process, the cloacal membrane, the prochordal plate and the allantois can be accepted as trustworthy and is entitled to its fair share of weight.

SUMMARY.

(1) The Embryo H.R.1 is at approximately the same stage of development as Grosser's H.Schm.10. It is at a later stage than the Strahl-Beneke and the T.F., and at an earlier stage than the Embryo Hugo.

(2) The curvature of the shield is the result of a growth process, although it may have been slightly exaggerated post-mortem. It is regarded as an indication of abnormal growth due, in part at least, to the shape of the chorionic cavity.

(3) The primordium of the head process is present and exhibits an early stage of development. It consists of a group of columnar cells which replace the entodermal roof of the yolk-sac over a limited area.

(4) The allantois is represented by a solid entodermal cord, which is regarded as the normal condition of the first stage of this structure.

(5) The primordium of the prochordal plate is present. It is suggested that at a later stage the plate plays some part in the formation of the buccopharyngeal membrane.

(6) The cloacal membrane is situated beyond the caudal end of the shield. It is suggested that the membrane normally develops first in this situation and then extends cranially to involve the shield.

(7) The primitive streak does not extend to the caudal limit of the shield. An early stage in the development of Hensen's node is described.

(8) A precociously developed coelomic space is present in the cranial part of the shield. The appearances suggest that the space communicates caudally with the exocoelom.

(9) Evidence is advanced in support of the view that the implantation cavity is enlarged by the incorporation within it of the large venous sinuses which are found in close proximity to the ovum.

(10) It is suggested that there is practically no circulation in the intervillous space at this stage. Evidence is advanced to show that as the arterioles are destroyed they are obliterated and do not open into the intervillous space, which is dependent for its inflow on capillaries in the decidua capsularis.

(11) The presence of a great number of large veins leading away from the venous sinuses and so from the intervillous space is regarded as a provision to ensure free outflow from the space when free circulation through it is established.

REFERENCES TO THE LITERATURE.

Barthelmez, G.W.	(1931)	The Human Uterine Mucous Membrane during Menstruation. American Journ. Obst. and Gynaecol. Vol.XXI.
Beneke, R. and Florian, J.	(1931)	Neue Befunde am Embryo 'Beneke' Anat. Anzeiger. Erganzungsheft zum Bd.71.
Bryce, T.H.	(1908)	Early Development and Imbedding of the Human Ovum. Glasgow.
	(1924)	Observations on the Early Development of the Human Embryo. Trans. Roy. Soc. Edinburgh Vol. LIII Pt.III
Corning, H.K.	(1925)	Lehrbuch der Entwickelungsgeschichte des Menschen. 2 Aufl. Bergman, München.
Daron, G.H.	(1936)	The arterial pattern of the tunica mucosa of the uterus in Macacus Rhesus. American Journal of Anatomy. Vol.58.
Falkiner, N.M.	(1932)	A Description of a Human Ovum fifteen days old, with special reference to the Vascular arrangements and to the Morphology of the Trophoblast. Journal Obst. and Gynaecol. of the British Empire. Vol.39.
Fetzer, M. and Florian, J.	(1929)	Der jüngste menschliche Embryo (Embryo 'Fetzer') mit bereits entwickelter Kloakenmembran. Anat. Anzeiger. Bd.67.
	(1930)	Der Embryo Fetzer. Zeitsch. f. Mikroscop. Anat. Forschung. Bd.21.

Florian, J.	(1928a)	Eine junges menschliche Ei in situ. (Embryo T.F. mit Primitivstreifen ohne Kopffortsatz) Zeitsch. f. Mikroskop. Anat. Forschung. Bd 13.
	(1928b)	Uber das Syncytium im Trophoblast junger menschlicher Embryonen. Anat. Anzeiger. Ergansungsheft zum Bd 66.
Florian, J. & Volker, O.	(1929)	Uber die Entwickelung des Primitivstreifens der Kloakenmembran und der Allantois beim Menschen. Zeitsch. f. Mikroskop. Anat. Forschung. Bd 16.
Florian, J.	(1933)	The Early Development of Man, with special reference to the Development of the Mesoderm and Cloacal Membrane. Journ. of Anat. Vol. LXVII.
Grosser, O.	(1913)	Ein menschlicher Embryo mit Chorda Kanal. Anat. Hefte Bd 47.
	(1931a)	Der Kopffortsatz des Primitivstreifens beim Menschen: seine Differenzierung bei dem Embryo. Wa.17. Zeitsch. f. Anat. und Entwickelungs. Bd 94.
	(1931b)	Primitivstreifen und Kopffortsatz beim Menschen. Anat. Anzeiger. Erganzungsheft zum Bd 71.
	(1931c)	Weiteres über den Primitivstreifen des Menschen. Anat. Anzeiger. Erganzungsheft zum Bd 72.
Hamilton, W.J.	(1937)	The early stages in the development of the Ferret. Trans. Roy. Soc. Edinburgh. Vol.LIX. Part 1.

Hertig, A.T.	(1935)	Angiogenesis in the Early Human Chorion and in the Primary Placenta of the Macaque Monkey. Contribs. to Embryology. Vol.XXV.
Hill, J.P. and Florian,J.	(1931)	A Young Human Embryo (Embryo Dobbin) with Head Process and Prochordal Plate. Phil.Trans. Roy. Soc. London. Series B. Vol.219.
	(1935)	An Early Human Embryo (No. 1285 Manchester Collection) with capsular attachment of the Connecting Stalk. Journ. of Anatomy, Vol.LXIX.
Ingalls, N.W.	(1918)	A Human Embryo before the appearance of the Myotomes. Contribs. to Embryology, No.23. Vol.VII.
MacIntyre, D.	(1926)	The Development of the Vascular System in the Human Embryo prior to the Establishment of the Heart. Trans. Roy. Soc. Edinburgh. Vol.LV. Pt.1.
Meyer, P.	(1924)	Ein junges menschliches Ei mit 0.4 mm Langen Embryonalschild. Archiv. f. Gynackol. Bd 122.
v. Möllendorff, W.	(1921a)	Uber ein junger, operativ gewonnen menschlichen Keim (Ei O.P.) Zeitsch. f. Anat. and Entwickelungs. Bd 62.
	(1921b)	Uber das jungste bisher bekannte menschliche Abortivei (Ei Sch.) Zeitsch. f. Anat. und Entwickelungs. Bd 62.
	(1925)	Das menschliche Ei WO (1fring). Zeitsch. f. Anat. und Entwickelungs. Bd 76.

Odgers, P.N.B. (1936) An Early Human Ovum (Thomson) in situ. Journal of Anatomy, Vol.LXXI.

Rabl, C. (1915) Edward van Beneden und der gegenwärtige Stand der wichtigsten von ihm behandelten Probleme. Archiv. f. Mikroskop. Anat. Bd 88.

Ramsey, E.M. (1937) The Lockyer Embryo; an early Human Embryo in situ. Contribs. to Embryology. Vol.XXVI.

Rossenbeck, H. (1923) Ein junges menschliches Ei. Ovum humanum Peh.1 - Hochstetter. Zeitsch. f. Anat. und Entwickelungs. Bd 68.

Sandison, J.C. (1932) Contraction of Bloodvessels and Observations on the Circulation in the Transparent Chamber in the Rabbit's Ear. Anat. Record. Vol.54.

Schauinsland, H. (1902) Article in Hertwig's Handbuch,1.

Schlagenhaufer - and Verocay - (1916) Ein junges menschliches Ei. Archiv. f. Gynaekol. Bd 105.

v. Spee, Graf (1896) Neue beobachtungen über sehr frühe Entwickelungsstufen des menschliches Eies. Archiv. f. Anat. und Physiol. Anat.Abt.

Sternberg, H. (1927) Beschreibung eines menschlichen Embryos mit vier Ursegmenten usw. Zeitsch. f. Anat. und Entwickelungs. Bd 82.

Stieve, H. (1926) Ein 13½ Tage altes, in der Gebarmutter erhaltenes und durch Eingriff gewonnenes menschliches Ei. Morph. Jahrbuch. Bd 7.

Stieve, H.	(1936)	Ein ganz junges, in der Gebarmutter erhaltenes menschliches Ei. (Keimling Werner). Jahrbuch f. Morph. und Mikroskop. Anat. Bd 40.
Strahl, H. and Beneke, R.	(1910)	Ein junger menschlicher Embryo. Wiesbaden.
Streeter, G.L.	(1936)	Early stages of the Macaque Embryo. (Abstract in Anat. Record, Vol.67).
Thompson, P. and Brash, J.C.	(1923)	A Human Embryo with Head Process and commencing Archenteric Canal. Journal of Anatomy, Vol.58.
Wyburn, G.M.	(1937)	The Development of the Infraumbilical Portion of the Abdominal Wall, with Remarks on the Aetiology of Ectopia Vesicae. Journal of Anatomy, Vol.LXXI.

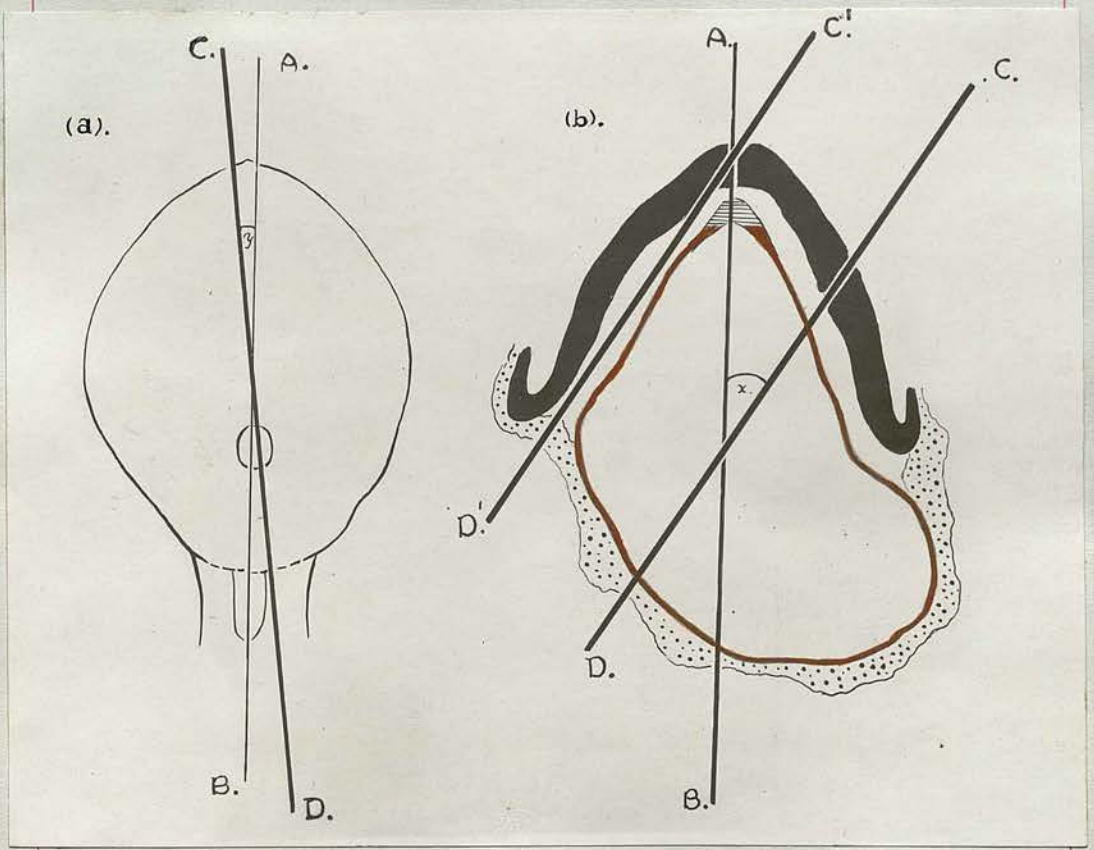

FIGURE 1.

(a): Schema of the dorsal projection of H.R.1. The line A.B. is the median plane and C.D. is the section plane. The angle 'y' = 5°. (X 100).

(b): Schema of a transverse section of H.R.1. The line A.B. is the median plane and C.D. is the section plane. The angle 'x' = 32.5°. The line C'.D'. represents approximately section 20.10. (X 200).

FIGURE 2.

The ovum in situ, showing the triangular shape of the chorionic cavity, the position of the embryo within the chorion, the villi and intervillous space and the large blood-clot which covers the surface of the decidua capsularis and obscures the point of entry. (X 17.9).

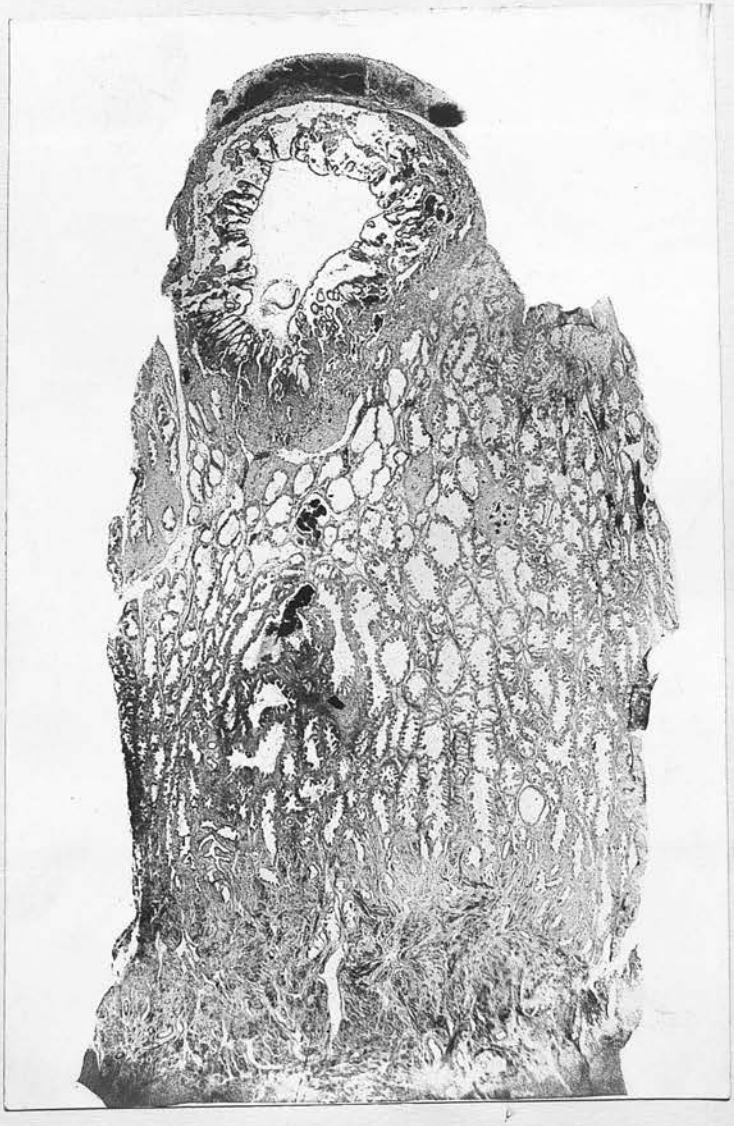

FIGURE 3.

The ovum in situ, showing the general appearance of the endometrium, and the superficial character of the implantation.

(X 11).

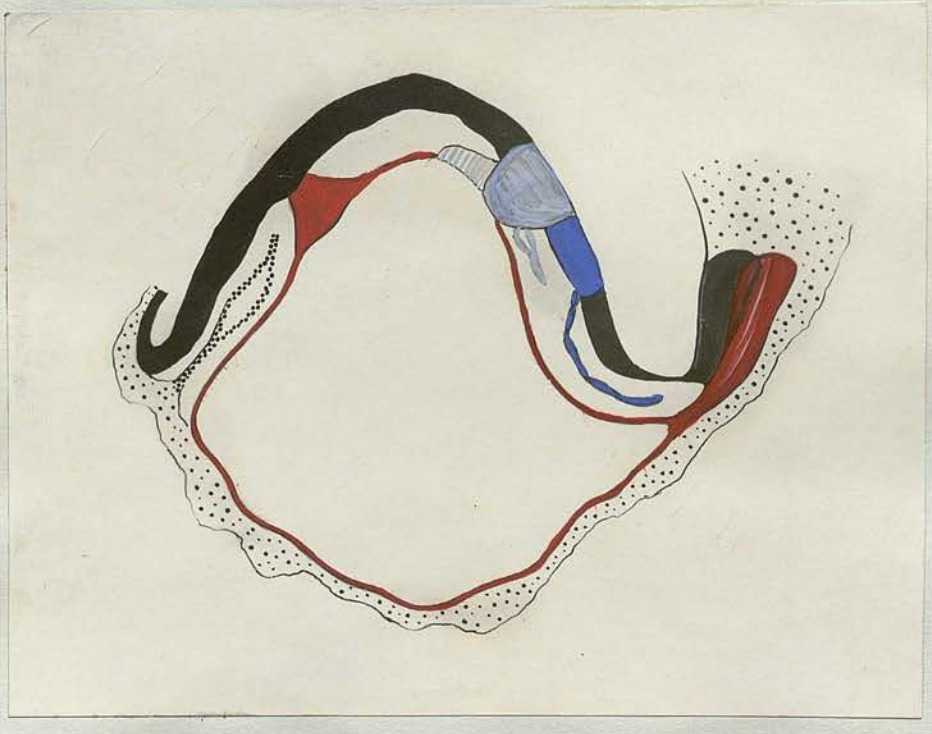

FIGURE 4.

A drawing of a median sagittal section of H.R.1 as determined by the reconstruction model. (X 200).

Undifferentiated ectoderm = black: Hensen's node = light blue: primitive streak = dark blue: head process = striped pale blue: primary mesoderm = light stipple: intra-embryonic mesoderm (in cranial region) = heavy stipple. The cloacal membrane is represented in the connecting stalk, where the entoderm of the solid allantoic cord blends with the amniotic ectoderm of the stalk.

FIGURE 5.

Description in text.

Section 18.1

(X 200).

FIGURE 6. Section 18.3

Description in text. (X 200).

FIGURE 7. Section 18.4

Description in text. (X 200).

FIGURE 8. Section 18.5

Description in text. (X 200).

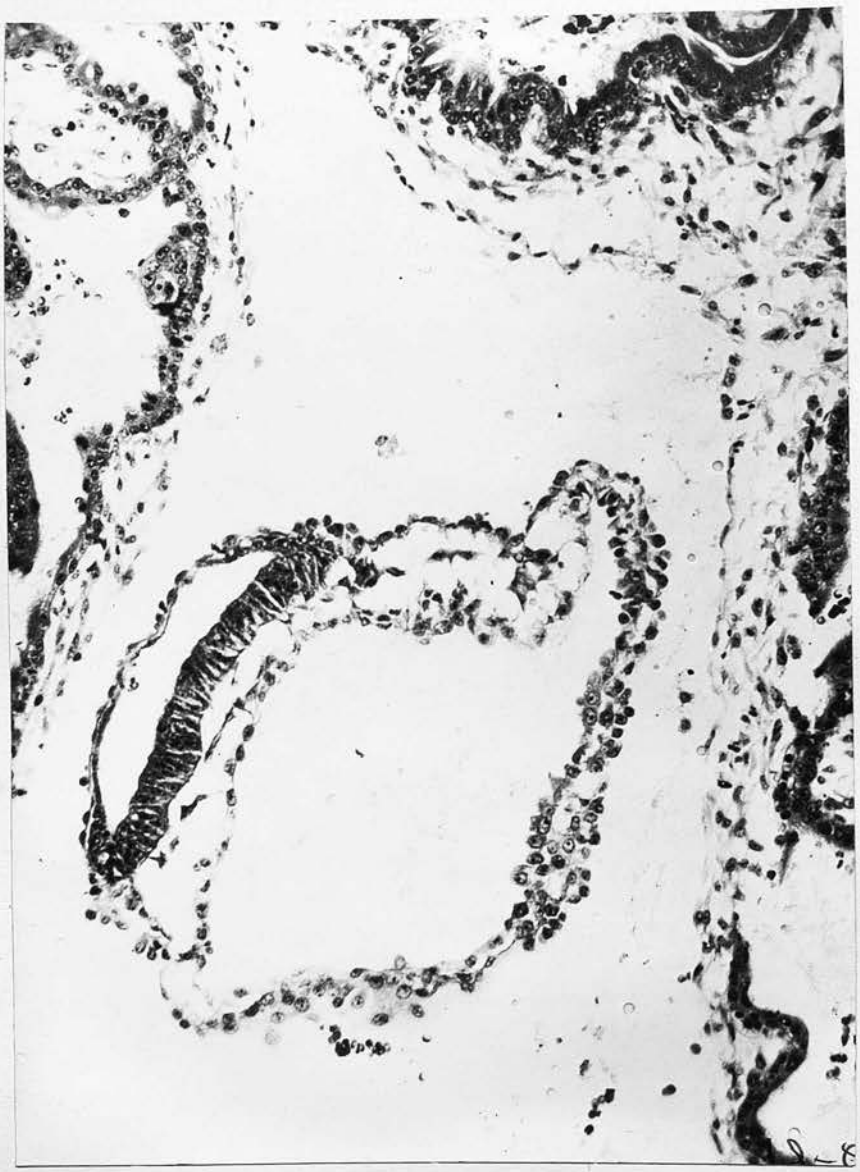

FIGURE 9. Section 18.6

Description in text. (X 200).

FIGURE 10. Section 18.8

Description in text. (X 200).

FIGURE 11. Section 18.9

Description in text. (X 200).

FIGURE 12. Section 18.10

Description in text. (X 200).

FIGURE 13. Section 18.11

Description in text. (X 200).

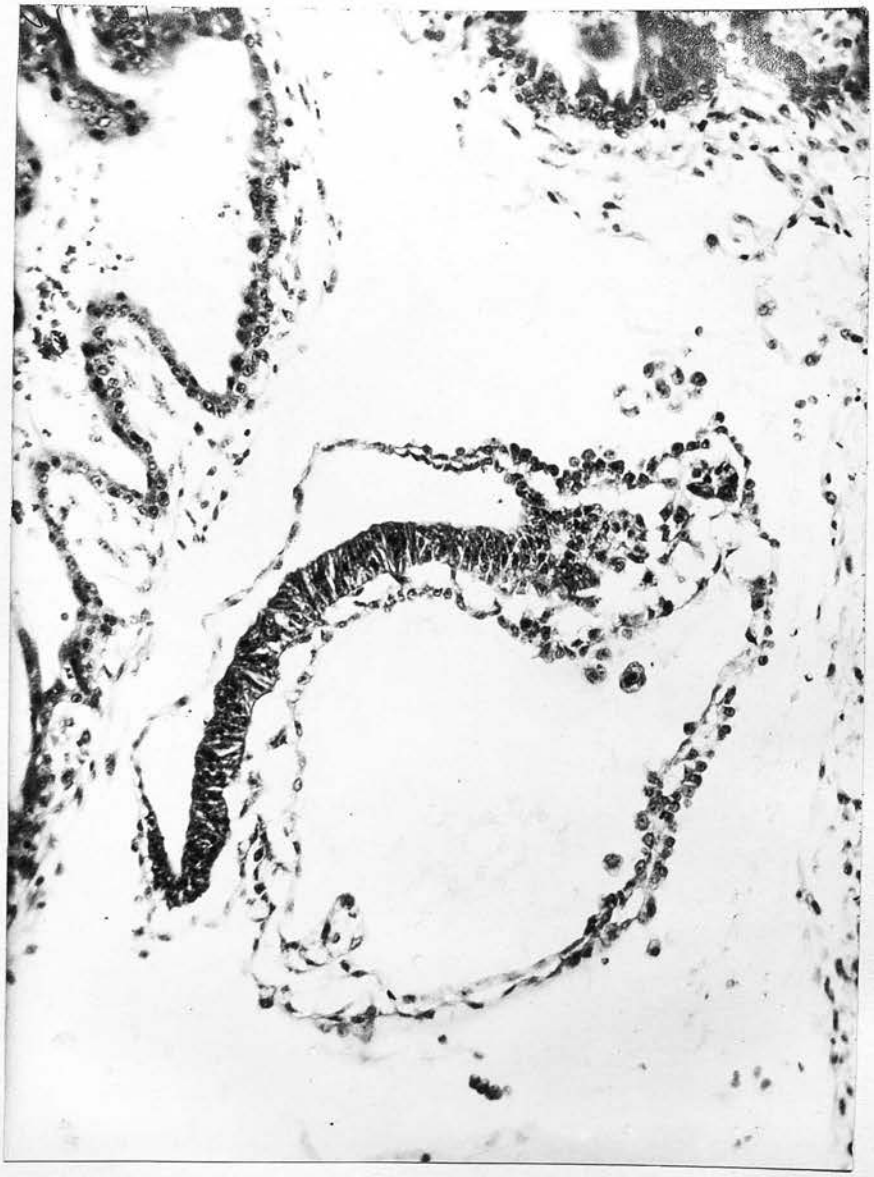

FIGURE 14. Section 18.12

Description in text. (X 200).

FIGURE 15. Section 19.1

Description in text. (X 200).

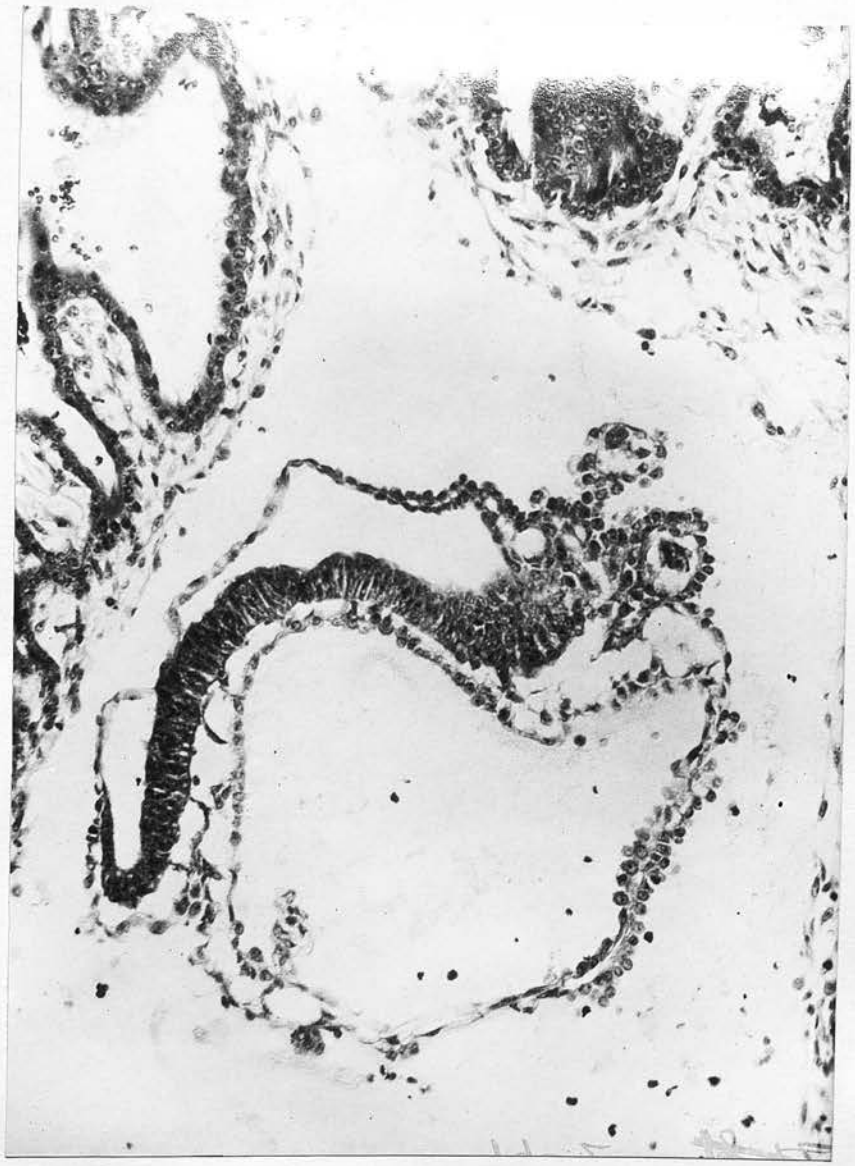

FIGURE 16. Section 19.2

Description in text. (X 200).

FIGURE 17. Section 19.3

Description in text. (X 200).

FIGURE 18. Section 19.4

Description in text. (X 200).

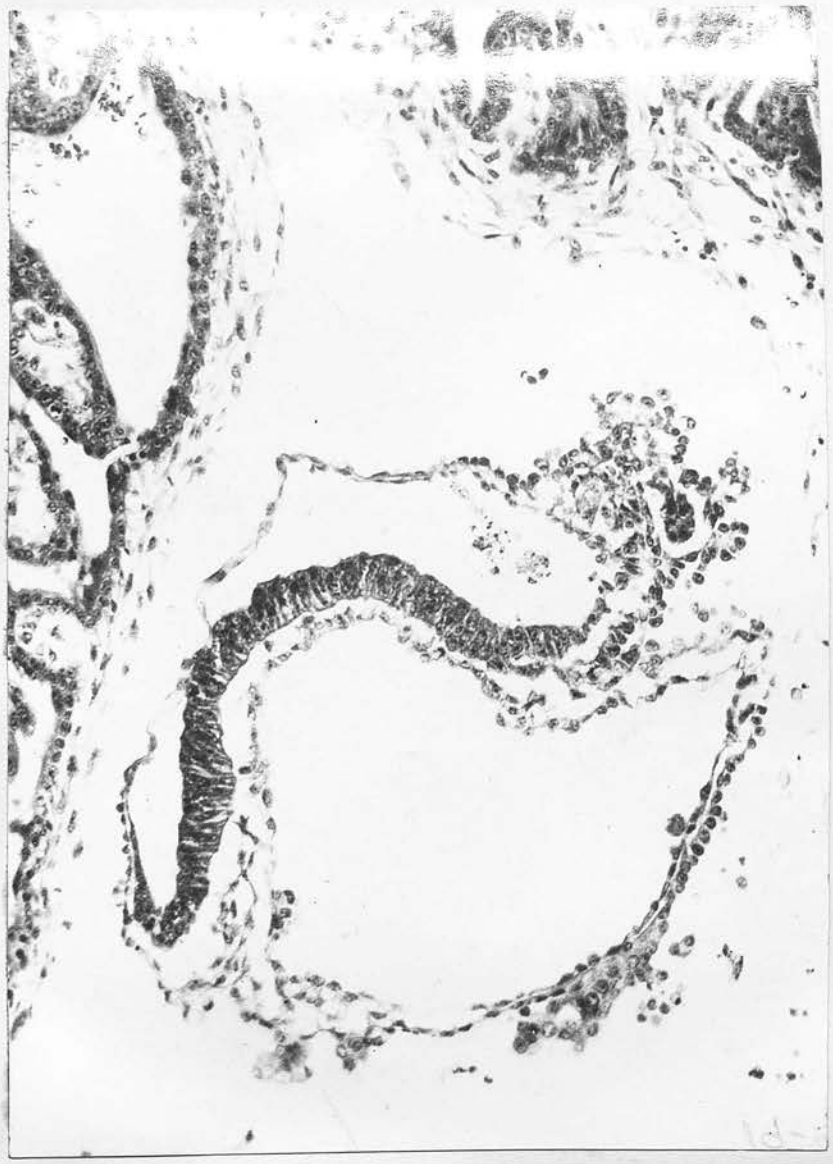

FIGURE 19. Section 19.5

Description in text. (X 200).

FIGURE 20. Section 19.6

Description in text. (X 200).

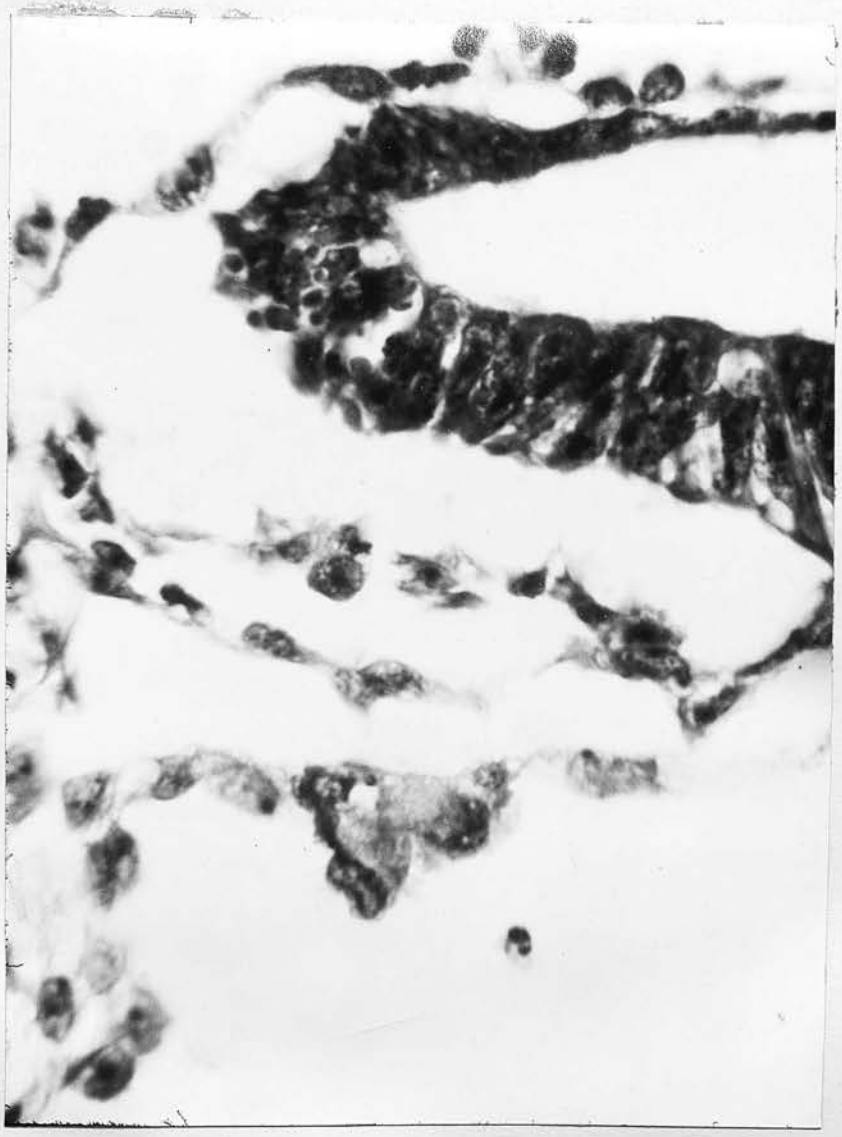

FIGURE 21. The cranial end of Section 19.6.

Description in text. (X 950).

FIGURE 22. Section 19.7

Description in text. (X 200)

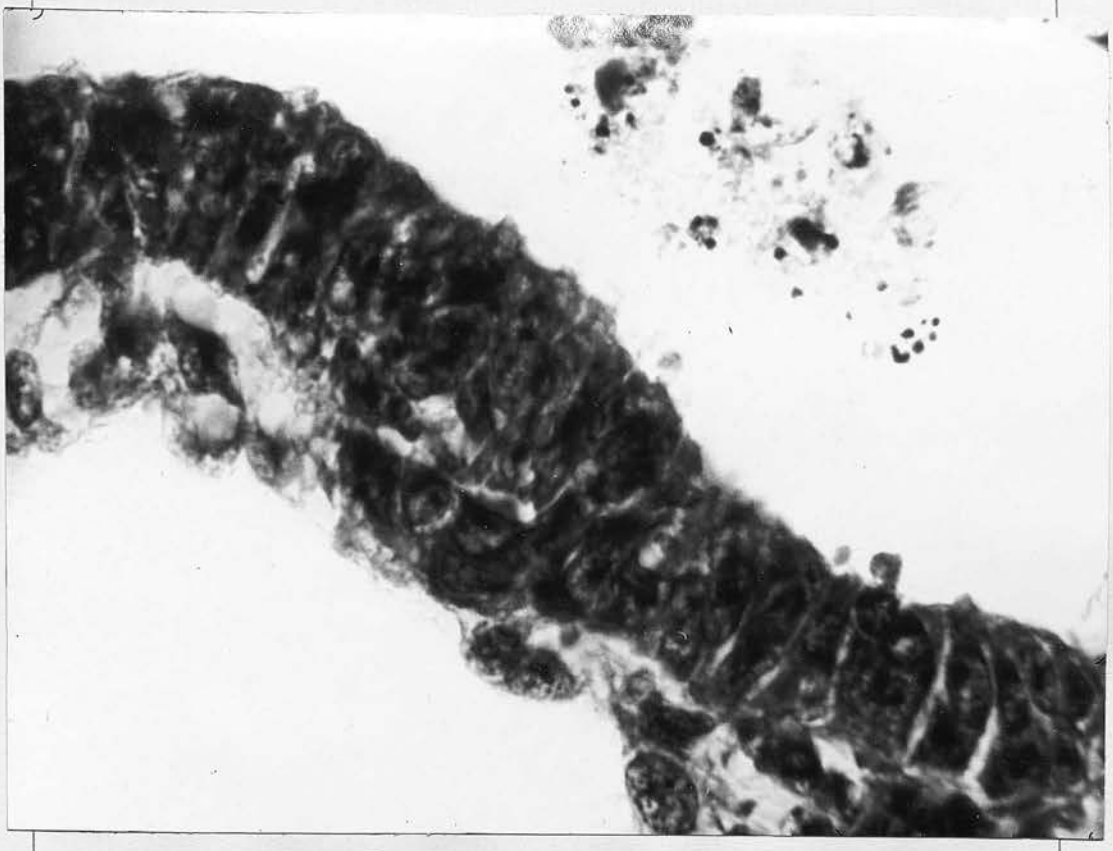

FIGURE 23. Part of Section 19.7.

Description in text. (X 950).

FIGURE 24. Section 19.8

Description in text. (X 200)

FIGURE 25. Section 19.9

Description in text. (X 200)

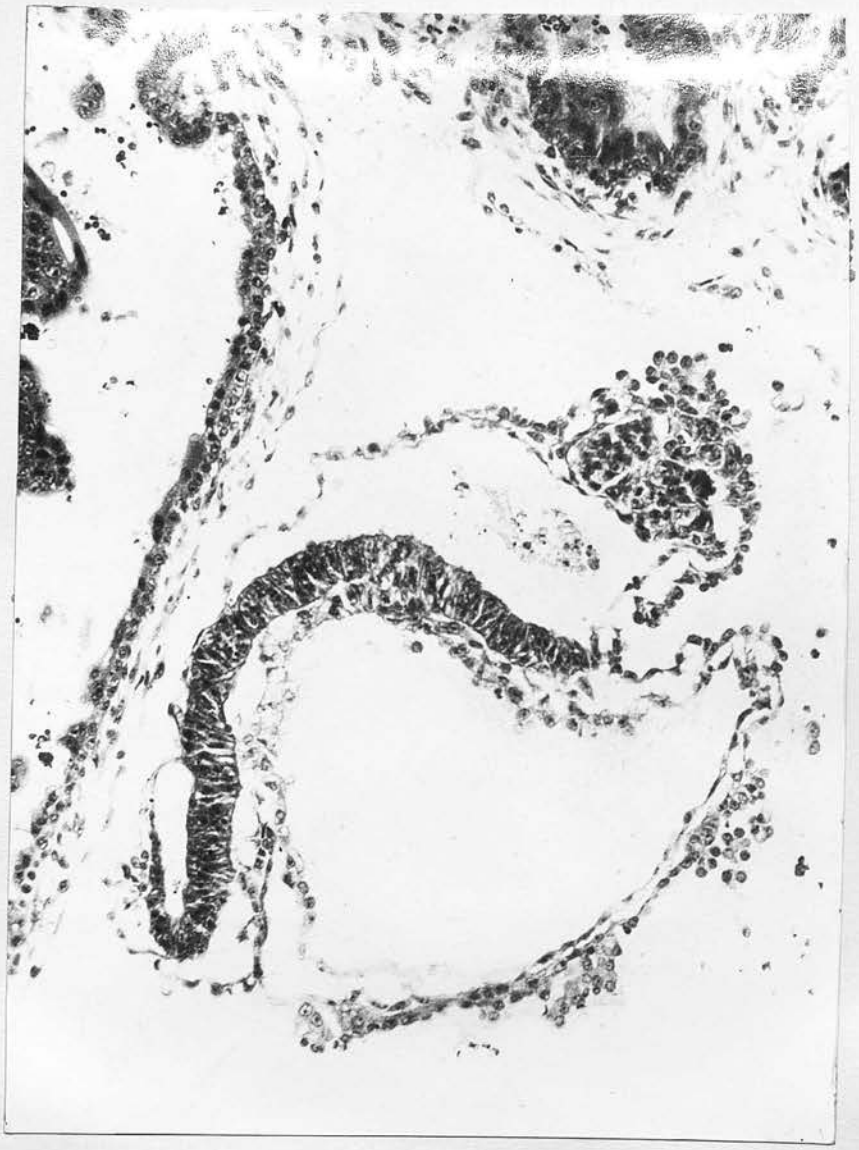

FIGURE 26. Section 19.10

Description in text. (X 200).

FIGURE 27. Section 19.11

Description in text. (X 200).

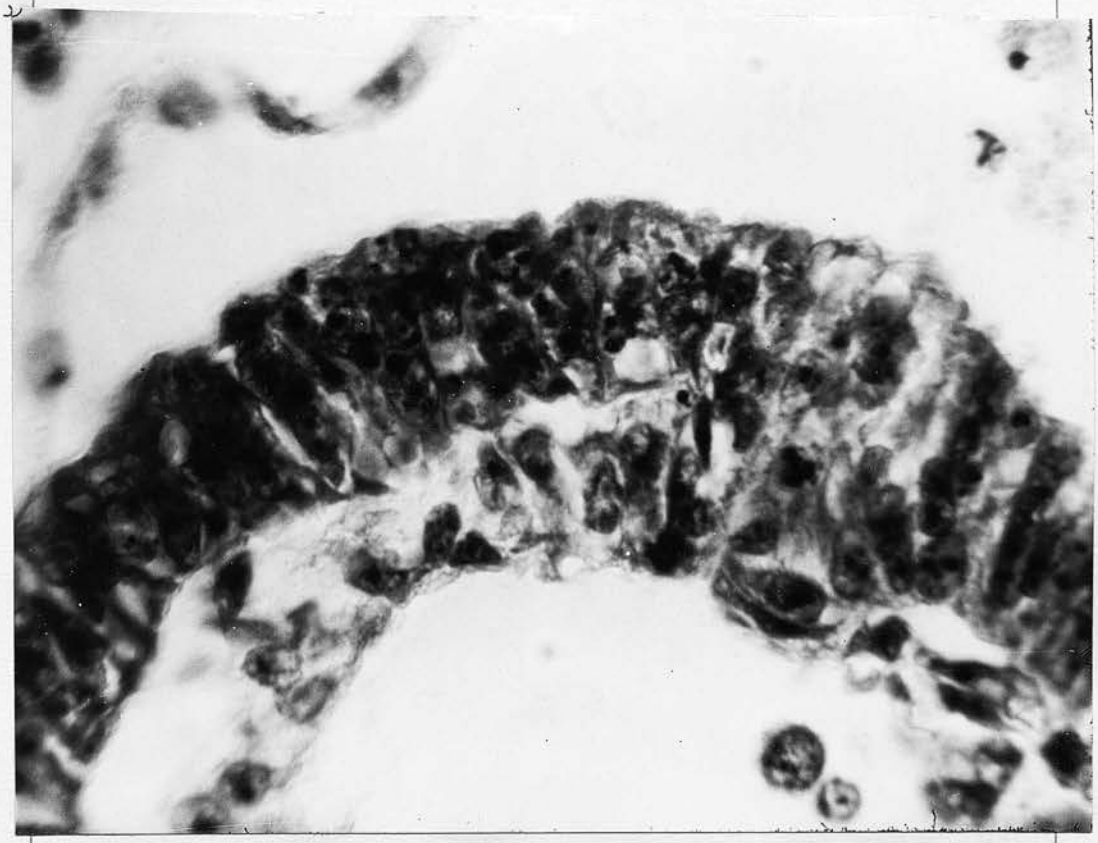

FIGURE 28. The region of Hensen's node in Section 19.11.

Description in text. (X 950).

FIGURE 29. Section 19.12

Description in text. (X 200).

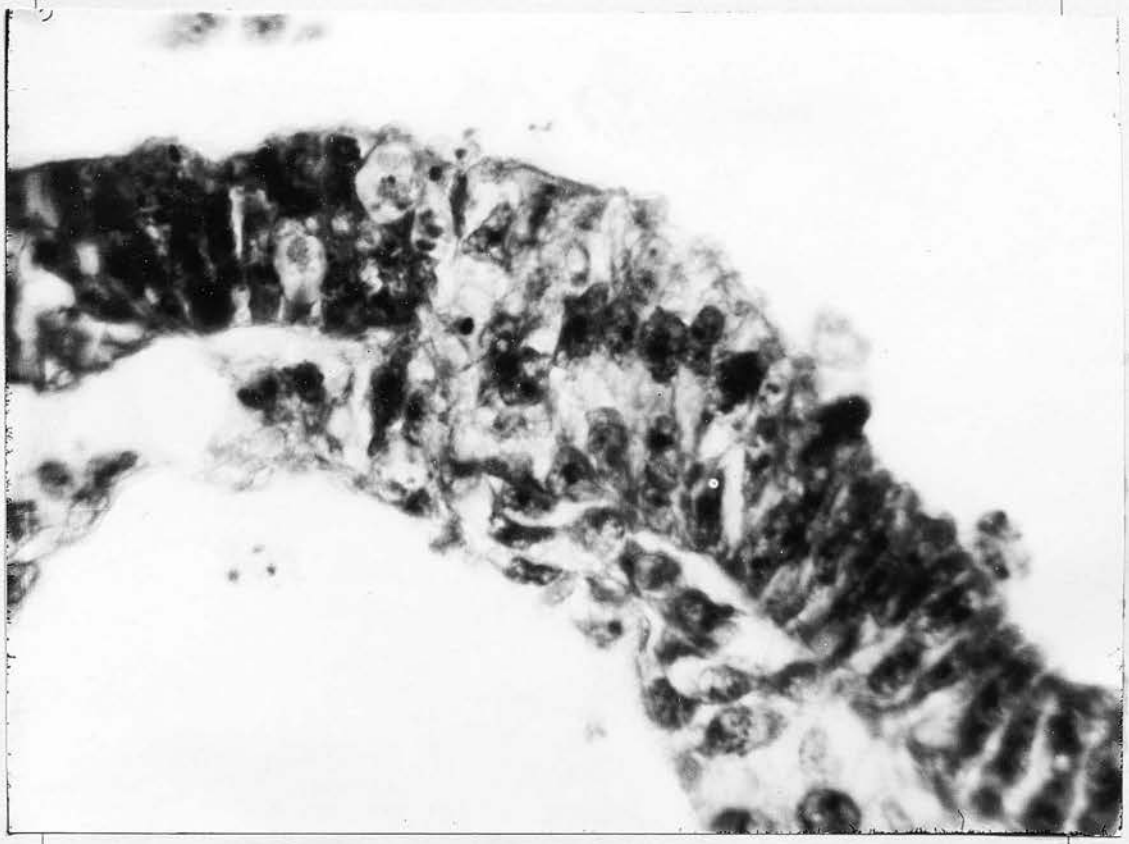

FIGURE 30. The region of Hensen's node in Section 19.12.

Description in text. (X 950).

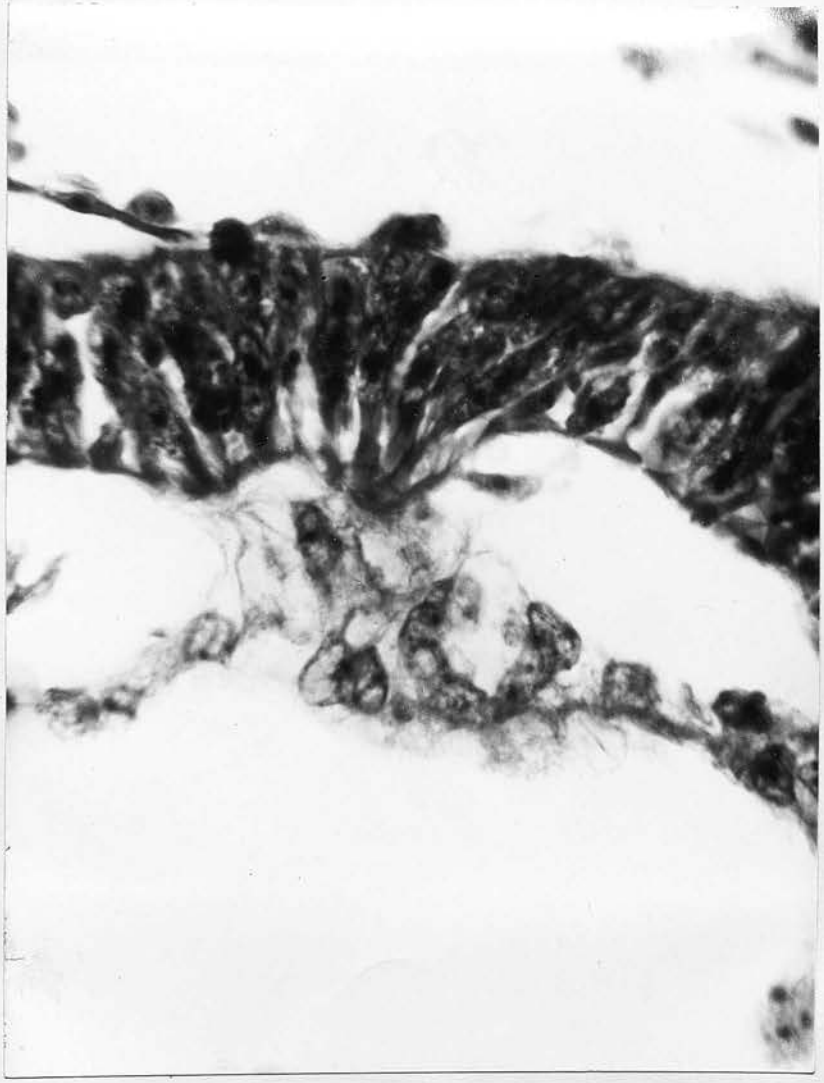

FIGURE 31. The primordium of the prochordal plate in Section 19.12.

Description in text. (X 950).

FIGURE 32. Section 20.1.

Description in text. (X 200).

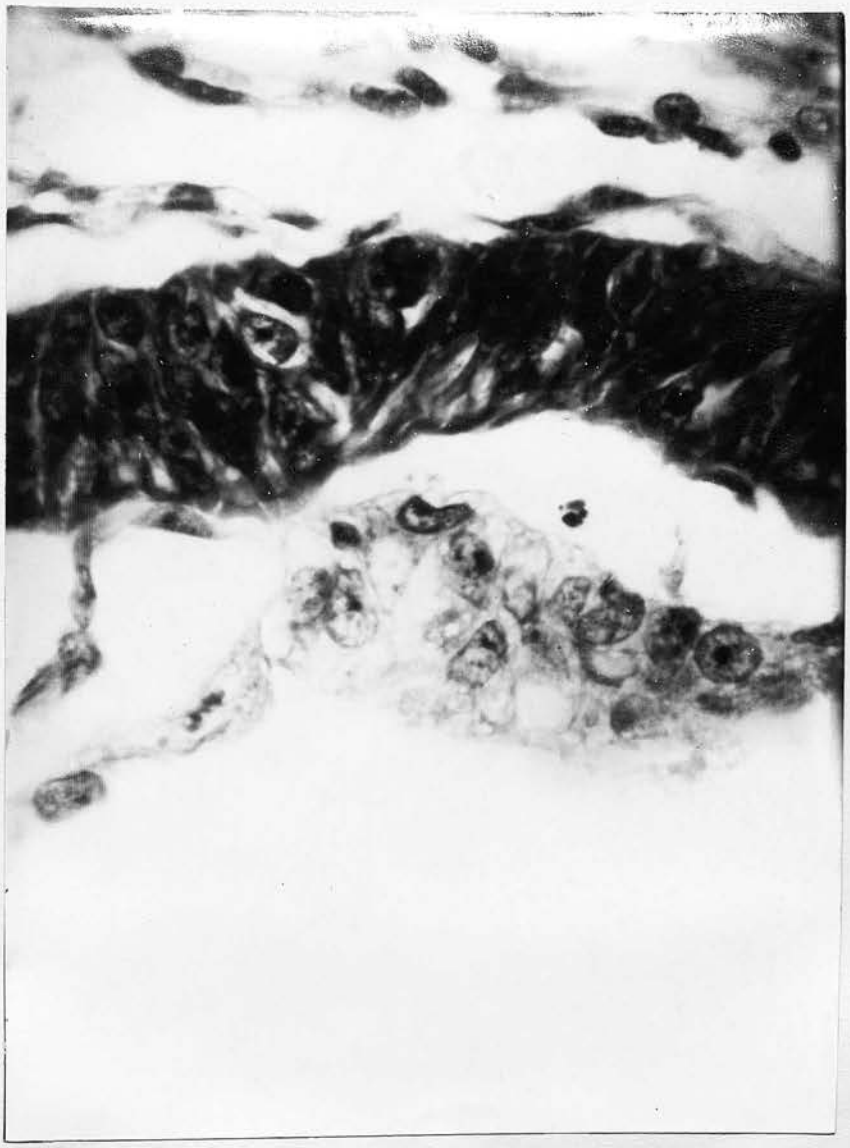

FIGURE 33. The primordium of the prochordal plate in Section 20.1.

Description in text. (X 950).

FIGURE 34. Section 20.2.

Description in text. (X 200).

FIGURE 35. Section 20.3

Description in text. (X 200).

FIGURE 36. Section 20.8

Description in text. (X 200).

FIGURE 37. Section 20.10

Description in text. (X 200).

FIGURE 38. Section 21.4

Description in text. (X 200).

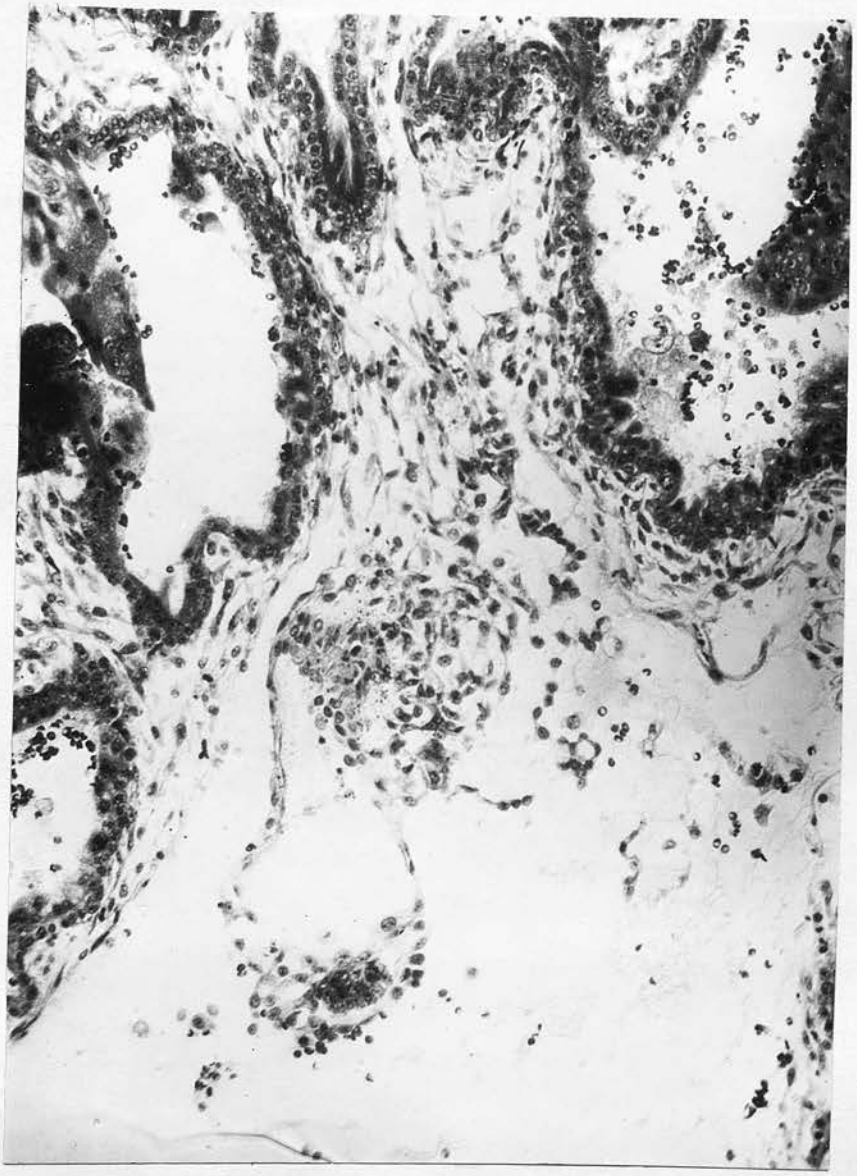

FIGURE 39. Section 21.10

Description in text. (X 200).

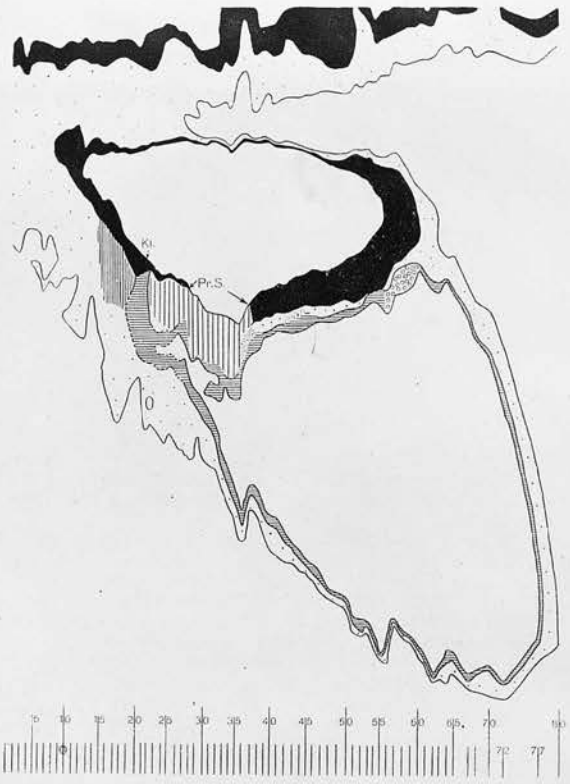

Abb. 1. Graphische Rekonstruktion des Medianschnittes durch den Embryo Beneke. Vergr. 1 : 150. Ektoderm schwarz. Entoderm waagerecht gestrichelt (das Gebiet, wo die Entodermzellen vesikulös sind, ist durch kleine Kreischen bezeichnet), primäres Mesoderm punktiert (wo es mit dem Entoderm der dorsalen Dottersackwand zusammengewachsen ist, sind die Punkte viel dichter gehalten und die Kontur des Entoderms ausgelassen), Primitivstreifen bei *Pr.S.* (das Axialmesoderm ist senkrecht gestrichelt; in seinem kaudalsten Abschnitte, wo es sehr kompakt gefügt ist, sind die Striche einander viel näher), Kloakenmembran bei *Kl.* — Die Schnittlinien der Medianebene mit den Ebenen der einzelnen Serienschnitte (die Nummern entsprechen jenen unter den Abbildungen in der ursprünglichen Beschreibung dieses Objektes vom Jahre 1910). (Die Entfernungen dieser Linien entsprechen den Zahlen, welche wir für die Schnittdicke durch unsere Messung bei den betreffenden Schnitten erhalten haben.)

FIGURE 40.

Professor Florian's graphic reconstruction of a median sagittal section through the Strahl-Beneke Embryo. Reduced to a magnification of just over 120.

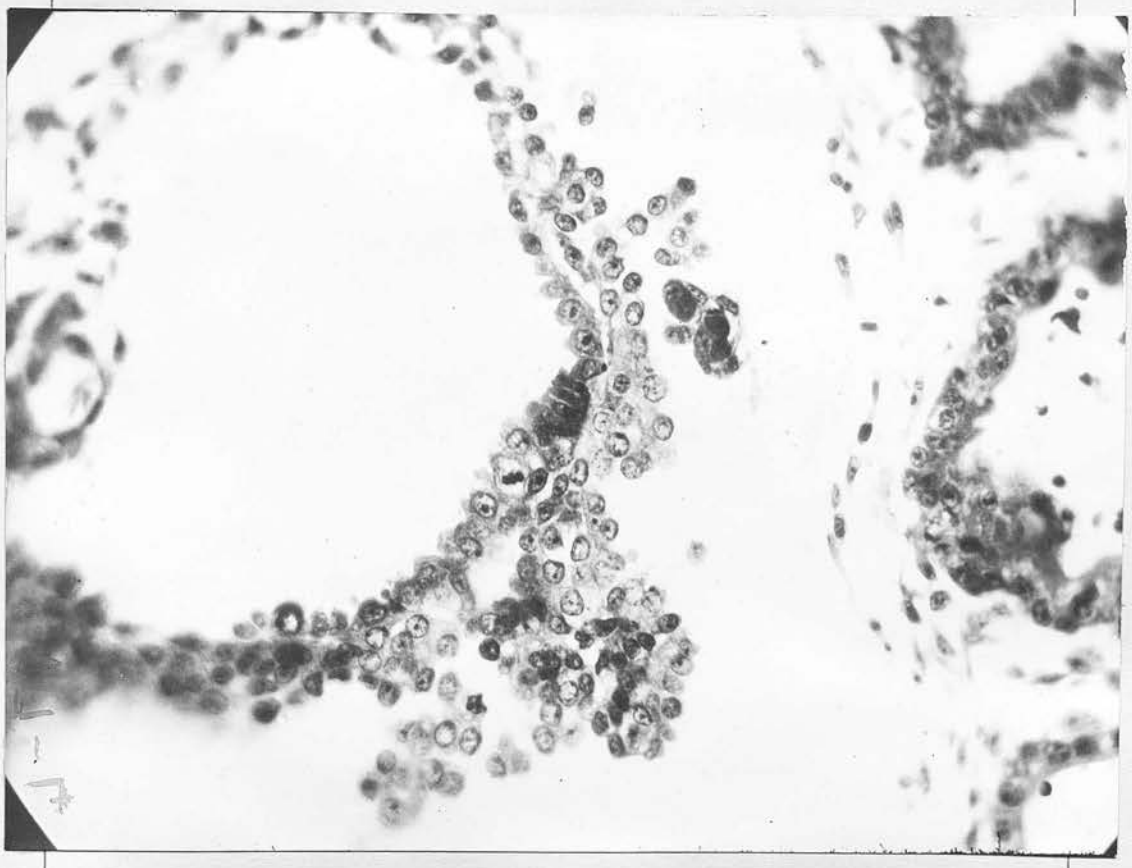

FIGURE 41.

A portion of the wall of the yolk-sac of H.R.1, showing a patch of typical, high columnar cells.

(X 392).

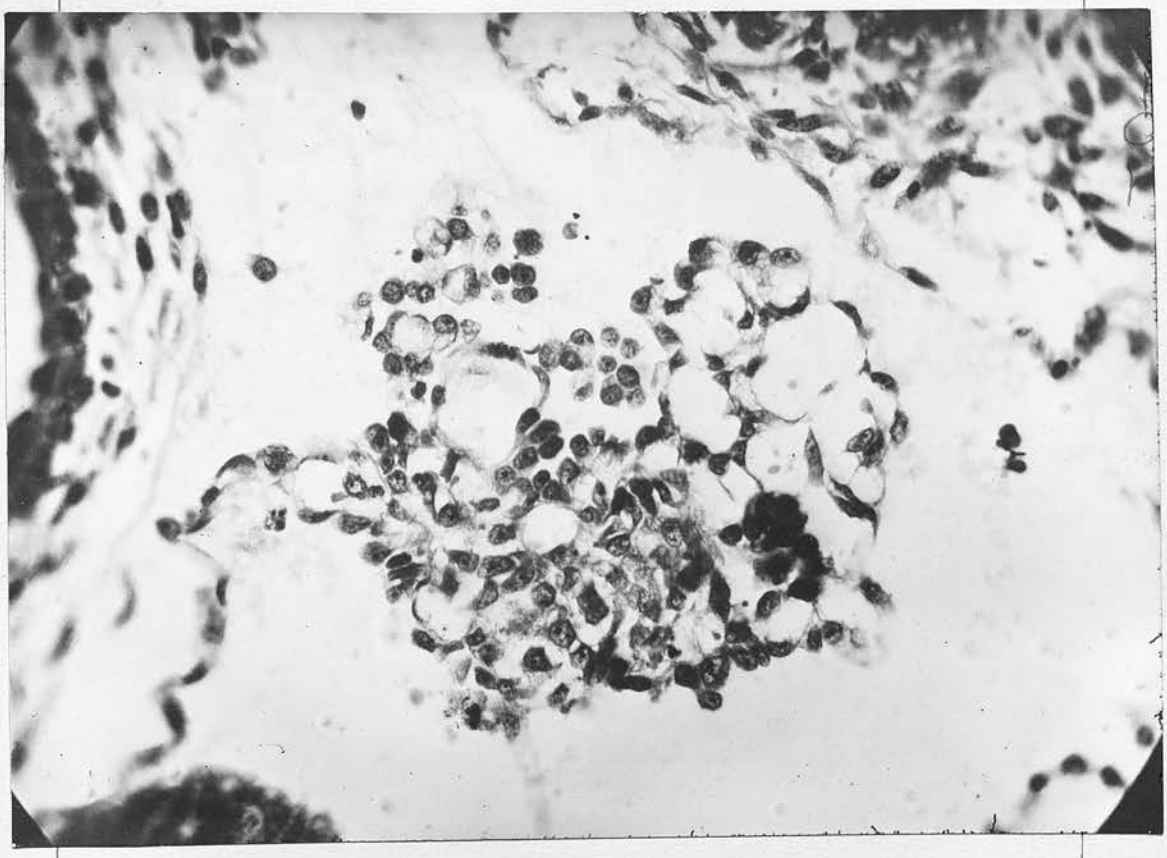

FIGURE 42.

The connecting stalk in Section 20.10, showing the presence of a large vascular space on the left side. (X 396).

FIGURE 43.

Primary mesenchyme of one of the villi.

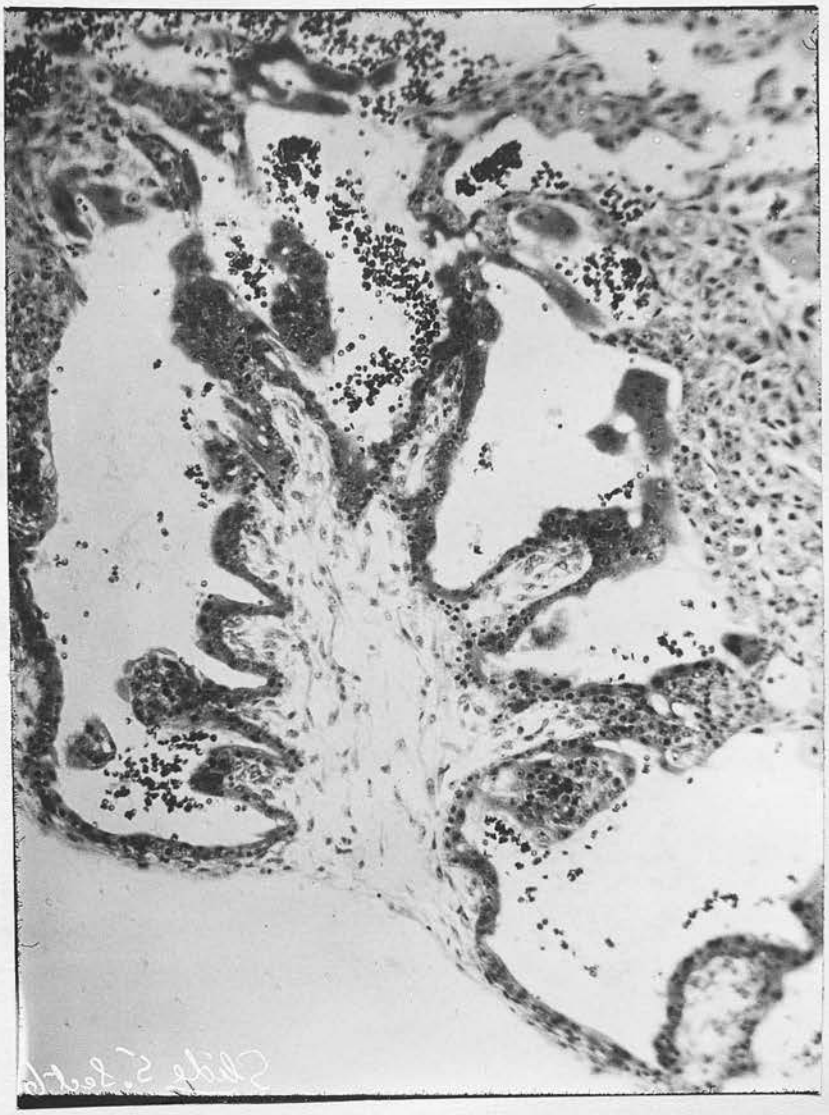

FIGURE 44.

One of the villi from the side wall of the chorion.

(X 154).

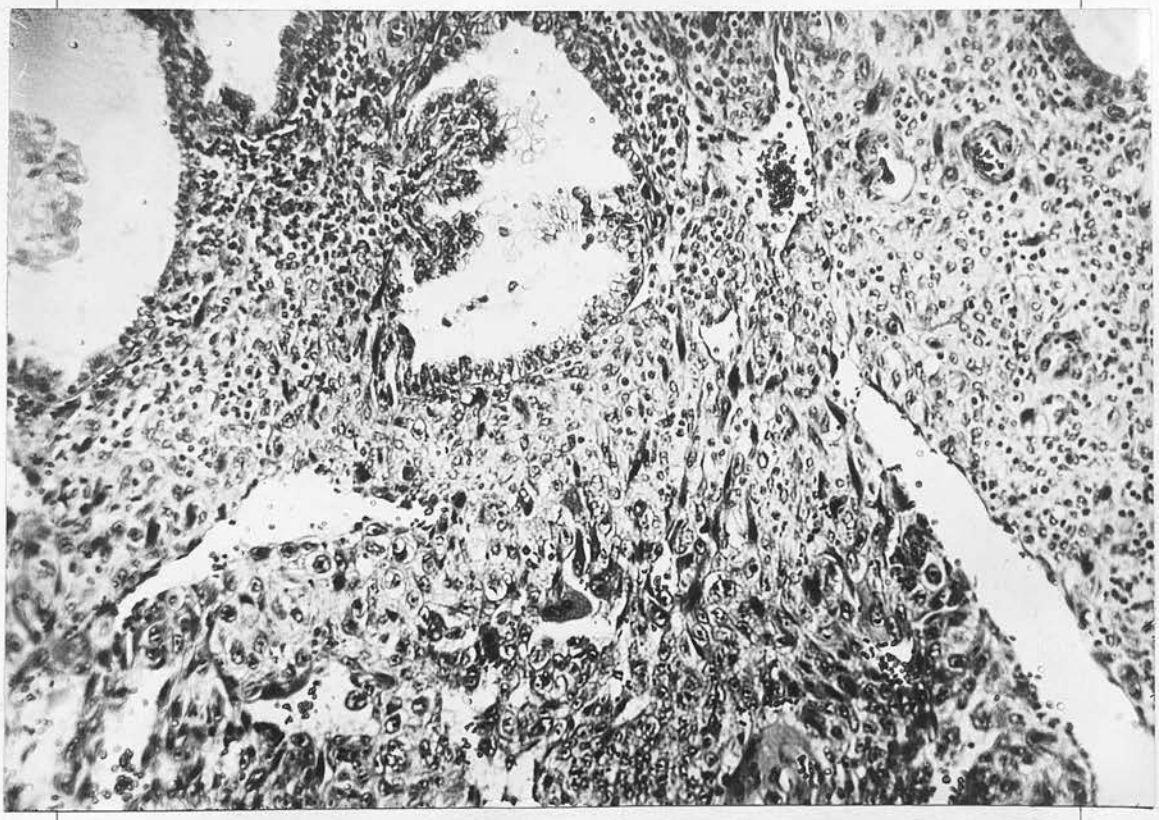

FIGURE 45.

A portion of the peripheral zone, showing in the lower part of the field the trophoblast shell, and in the middle of the field strands of the darkly staining proliferative plasmodium. (X 158).

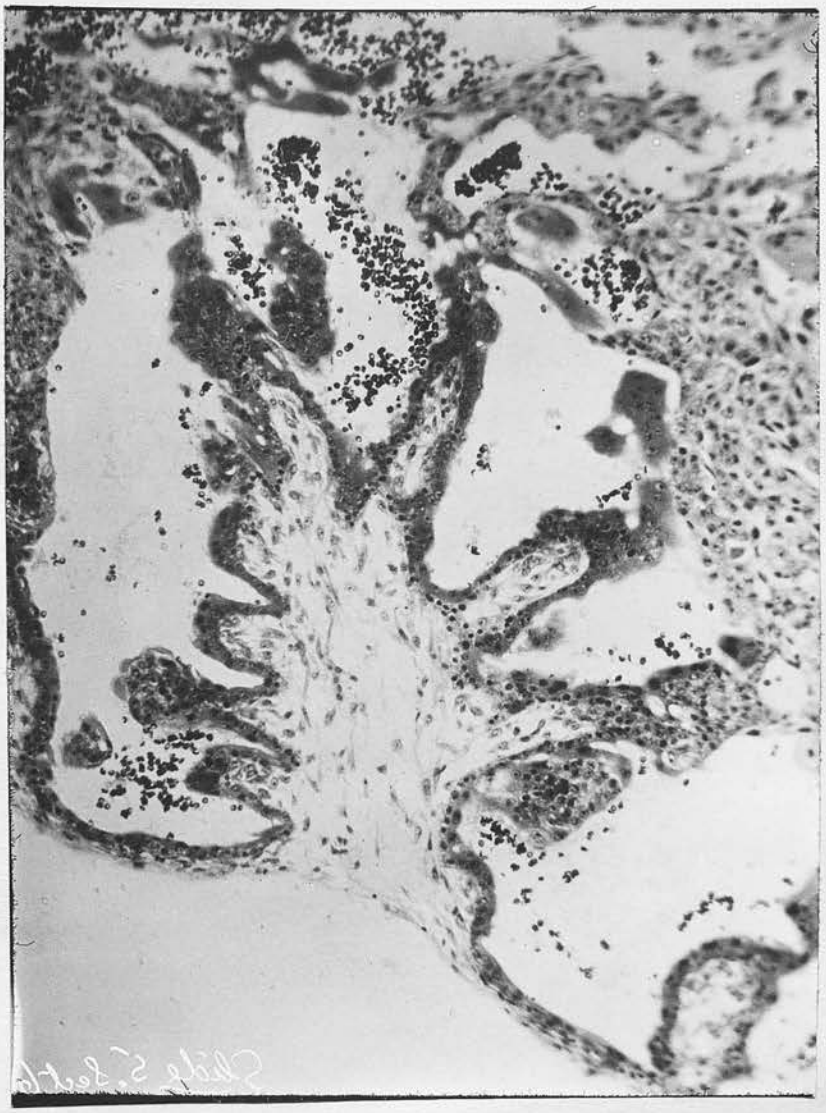

FIGURE 44.

One of the villi from the side wall of the chorion.

(X 154).

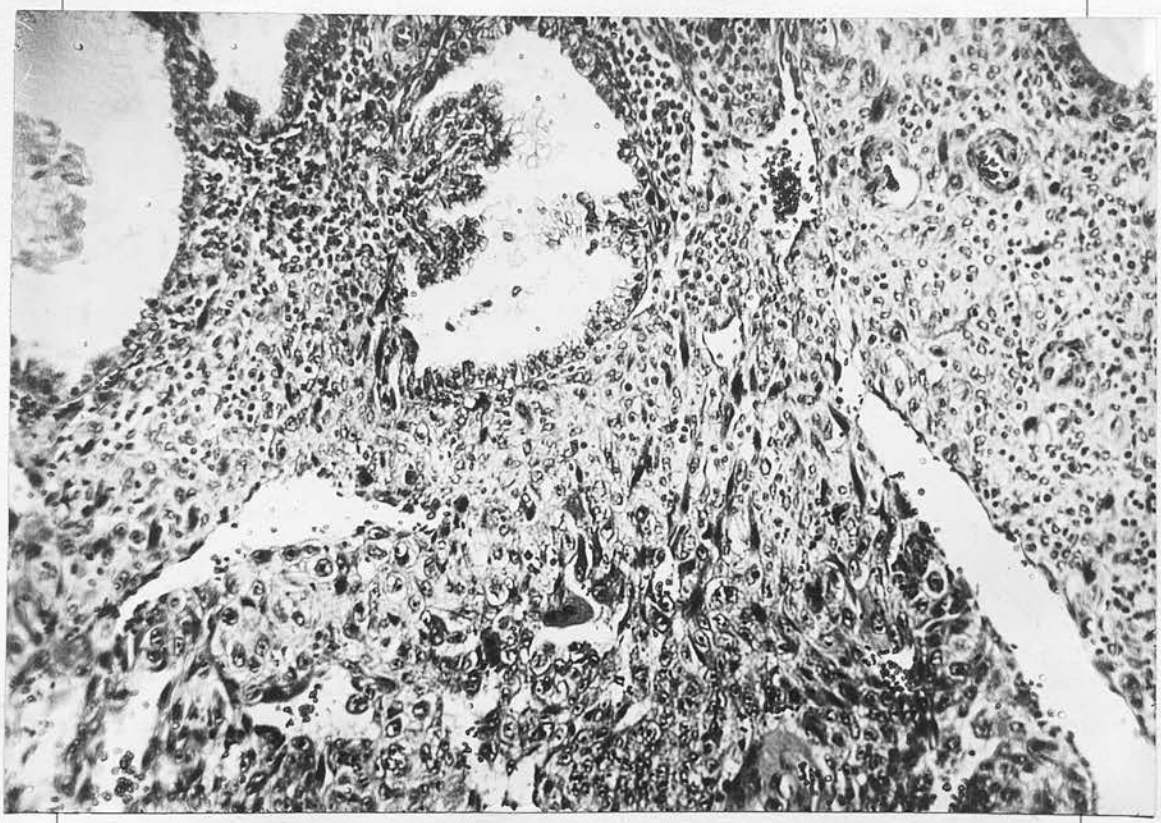

FIGURE 45.

A portion of the peripheral zone, showing in the lower part of the field the trophoblast shell, and in the middle of the field strands of the darkly staining proliferative plasmodium. (X 158).

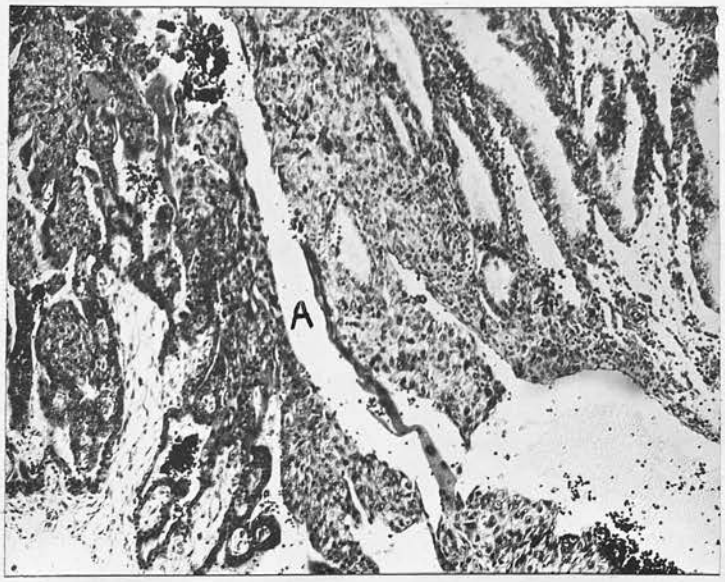

FIGURE 46.

A portion of the peripheral zone, showing one of the vascular spaces within the trophoblast shell lined with proliferative plasmodium (A.). (X 80).

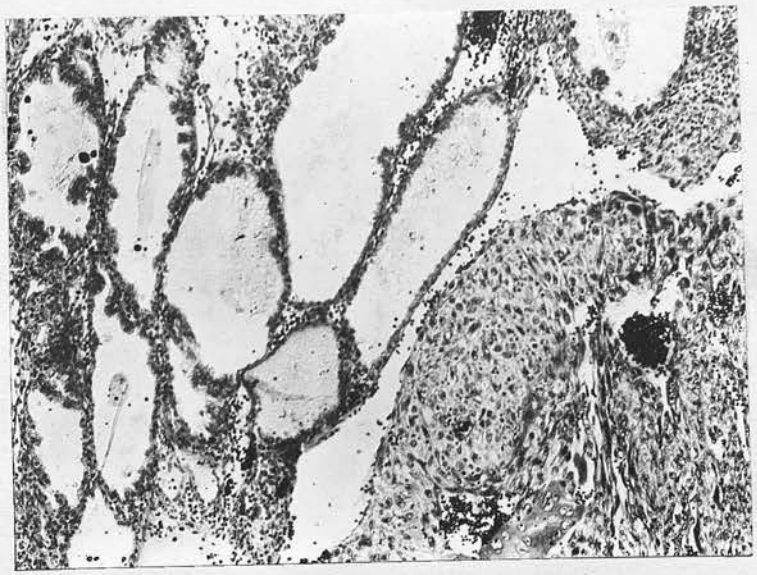

FIGURE 47.

The stratum spongiosum in the immediate neighbourhood of the ovum. A portion of the peripheral zone occupies the lower right-hand part of the field, to the left of which, and separated from it by a venous sinus, the glands are not only dilated but their walls are flattened and do not show the typical "saw-teeth" appearance of the epithelium. (X 80).

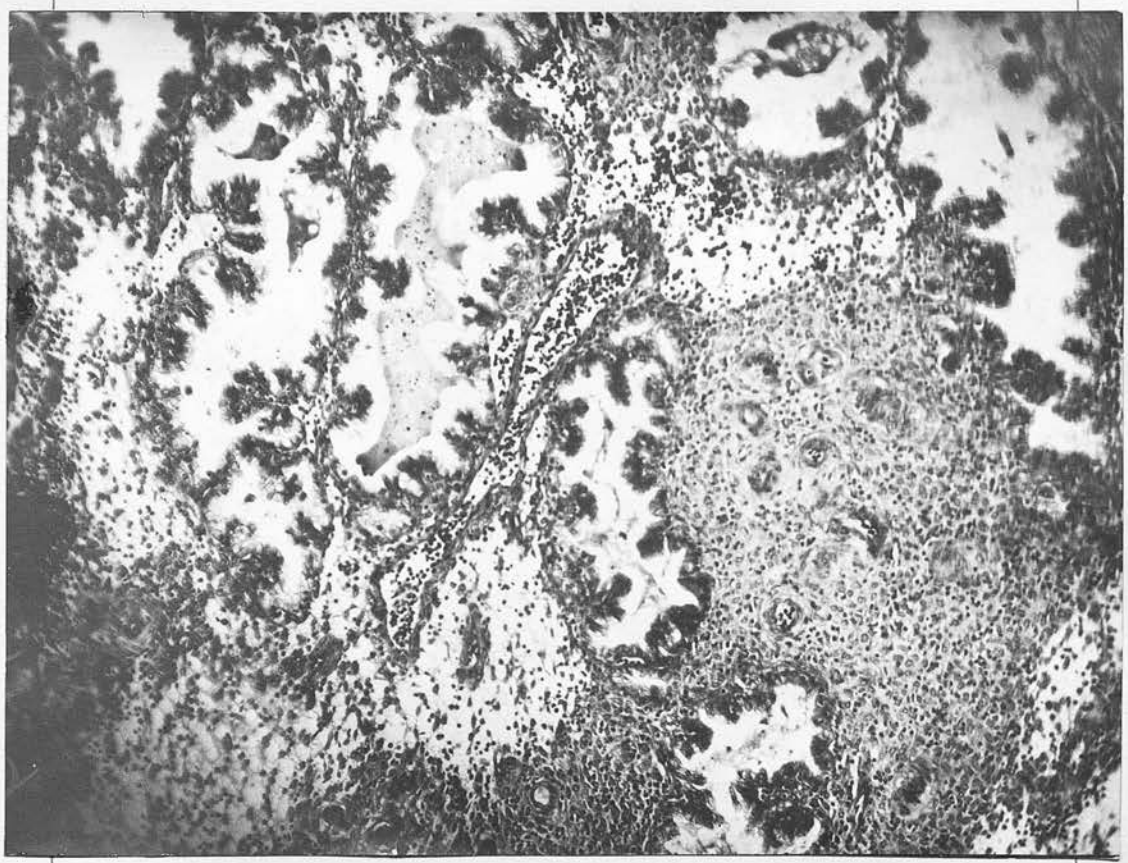

FIGURE 48.

A portion of the endometrium adjoining the ovum. A vein, cut in its long axis and full of white blood-corpuscles, is seen traversing a patch of oedema in the centre of the field. To its right a patch of non-oedematous stroma can be seen in which one of the 'cork-screw' arteries has been cut in many places. The walls of the artery are swollen and thickened. (X 101).

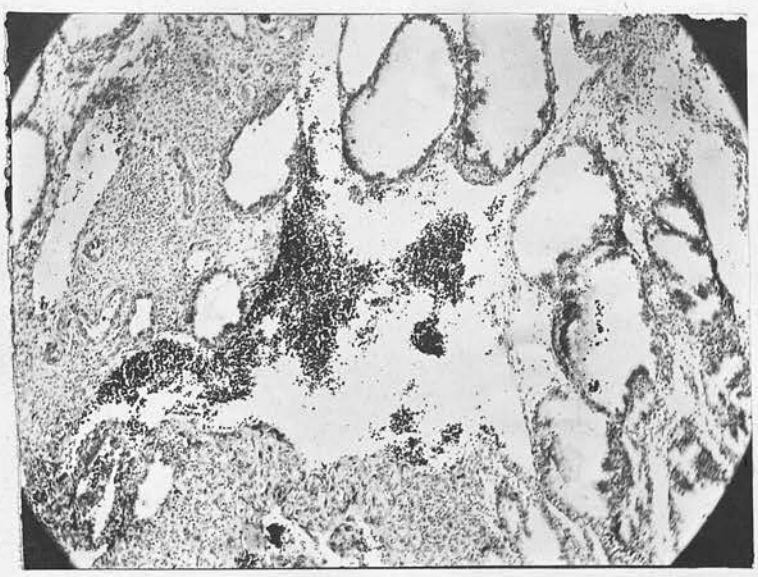

FIGURE 49.

A large venous sinus lying deep to the ovum. Three large veins arise from it and run into the deeper part (upper part, in the figure) of the endometrium. (X 80).

FIGURE 50.

Photograph of a drawing of a portion of the peripheral zone, showing one of the 'cork-screw' arteries (X) with swollen endothelial lining and partially obstructed by fibrinoid substance. Elements of the proliferative plasmodium are in intimate relation with the vessel wall.

Drawn by Miss P.M.Lariviere.

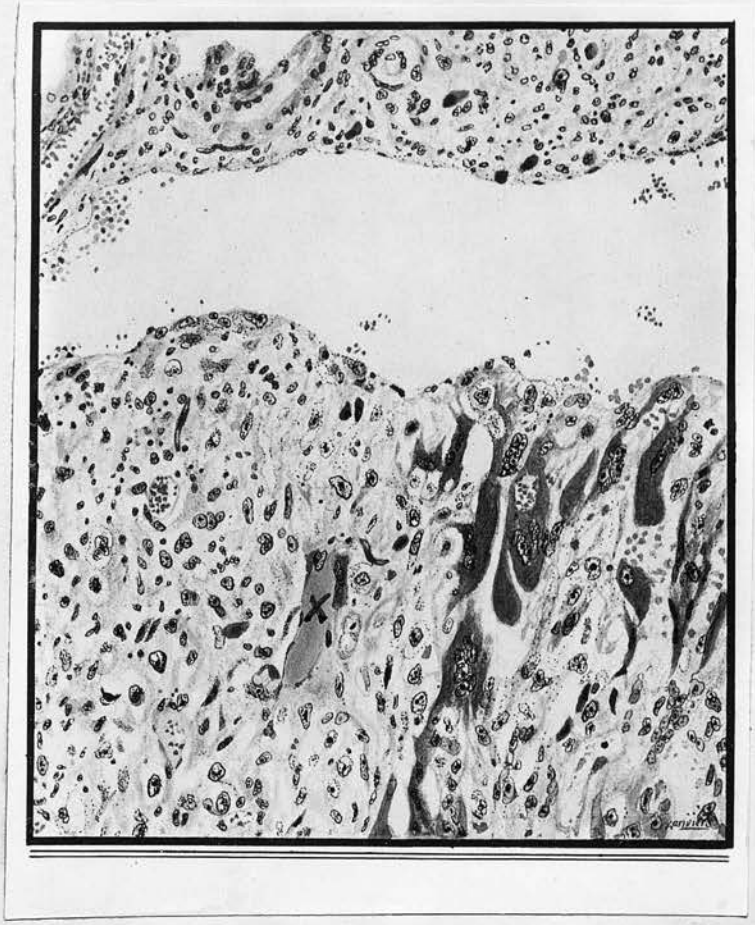

FIGURE 51.

Lower magnification of the same arteriole (X) a little distal to Figure 50, completely obstructed by fibrinoid substance. Elements of the proliferative plasmodium are seen in relation to the vessel wall, and also on the opposite side of the venous sinus which lies deep to the decidua basalis.

Drawn by Miss P.M.Lariviere.